Diplomarbeit

Effects of manual lymphatic drainage on hemodynamic responses

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Paul Simon

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Goswami, Nandu, Assoz. Prof. Priv.-Doz. Dr.med. MMedSci PhD.
Rössler, Andreas, Ao.Univ.-Prof. Mag. Dr.rer.nat.
Brix, Bianca, Dr.scient.med. BSc MSc

Graz, am 26.07.2021

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Graz, am 26.07.2021 *Paul Simon, eh.*

Acknowledgments

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List of abbreviations:

mBP: mean blood pressure

MAP: mean arterial pressure

sBP: systolic blood pressure

dBP: diastolic blood pressure

HR: heart rate

CO: cardiac output

SV: stroke volume

O_2: of oxygen

CO_2: carbon dioxide

BMI: Body Mass Index

kDa: kilodaltons

bpm: beats per minutes

ECG: electrocardiography

ATP: adenosine triphosphate

ET: endothelin

A.: arteria

V.: vena

N.: nervus

CDT: complete decongestive therapy

PO_2: oxygen partial pressure

PCO_2: carbon dioxide partial pressure

GFR: glomerular filtration rate

ICG: impendance cardiography

SD: standard deviation

SEM: standard error of the mean

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Zusammenfassung

Einleitung: Das Lymphsystem ist neben dem Kardiovaskulären System im menschlichen Körper das wichtigste Transportsystem. Bei Fehlregulationen dieses Systems kann es zu Ansammlung von Lymphflüssigkeit im Gewebe kommen und so zu Lymphödemen führen. Mit einigen tausend Betroffenen in Österreich, zählt dieses Symptom zu den häufigsten Leiden in der westlichen Bevölkerung. Da sich das Herz- und Lymphsystem in ständiger Zusammenarbeit befinden, lässt sich nur vermuten, dass bei einer Störung des einen Systems, das andere auch betroffen ist. Nach ausführlicher Beschreibung der Physiologie und Anatomie des Lymph- und Herzsystems, wird in dieser Arbeit auch die Pathophysiologie und Therapiemaßnahmen der Lymphödeme besprochen. Der Fokus liegt hierbei auf der manuellen Lymphdrainage. Weiters folgt die Beschreibung der Reaktion des Kardiovaskulären Systems auf Lageveränderungen des Körpers im Raum.

Ziele & Aufgaben: Diese Studie befasst sich mit der Untersuchung und Messung verschiedenster Vitalparameter von Patienten mit Lymphödemen, welche, während eines sit-to-stand Tests, jeweils vor und nach einer manuellen Lymphdrainage erhoben werden. Das Ziel ist es die Frage zu beantworten, ob eine vollständig entstauende Lymphödemtherapie die hämodynamischen Reaktionen beeinflusst.

Methoden: Insgesamt wurden 11 männliche und weibliche Patient*innen (57 ± 8 Jahre alt, 167,2 ± 8,3 cm groß, 91,0 ± 23,5 kg schwer) mit Lymphödemen der unteren Extremität im Stadium II für die Studie herangezogen. Die Behandlung des Lymphödems orientierte sich an den aktuellen Standards und wurde im Zentrum für lymphatische Erkrankungen in Wolfsberg durchgeführt. Sie besteht aus einer manuellen Lymphdrainage für 30 Minuten, gefolgt von der Anlage von Kompressionsverbänden. Die Vitalparameter wurden, während eines sit-to-stand Tests an unterschiedlichen Zeitpunkten (Epochen), sowie jeweils vor und nach der Lymphdrainage erhoben. Die erhobenen Werte (Herzrate, Herzauswurfrate, Schlagvolumen und Blutdruck) wurden mittels Elektrokardiografie, Plethysmographie und Impendanz Kardiographie gemessen. Diese Arbeit befasst sich nur mit den erhobenen Werten von Tag 1 der Studie.

Ergebnisse: Die meisten der erwarteten Unterschiede in den Parametern waren statistisch nicht signifikant. Es gab wiederkehrende Tendenzen zur Signifikanz in den Werten, welche aber zu gering ausfielen, um als signifikant bezeichnet zu werden. Lediglich die Herzfrequenz zeigte Signifikanz in Epoche 6 (von 94 auf 86 Schläge pro Minute ($p<0,001$)), Epoche 7 (von 92 auf 85 Schläge pro Minute ($p=0,059$)), Epoche 8 (von 93 auf 83 Schläge pro Minute ($p=0,008$)), Epoche 9 (von 90 auf 84 Schläge pro Minute ($p=0,044$)) und über alle Epochen ($F_{(9,72)}=2,53$; $p=0,014$). Signifikanz

wurde auch in den Epochen des Herzzeitvolumens erreicht ($F_{(9,18)}$=4,32; p=0,004).

Schlussfolgerungen: Die Ergebnisse der Vitalparameter, jeweils vor und nach der manuellen Lymphdrainage zeigten, dass die Therapie einen Einfluss auf die hämodynamische Reaktion hat, allerdings zu wenig um sie als signifikant zu bezeichnen. Die Hauptfaktoren für die veränderten Werte sind vermutlich das höhere verfügbare Volumen im Kreislaufsystem, sowie die verringerte Belastung des erkrankten Gewebes durch die Lymphödeme.

Abstract

Introduction: Besides the cardiovascular system, the lymphatic system is the most important transport system in the human body. Dysregulation of this system can lead to accumulation of lymphatic fluid in the tissue, resulting in lymphedema with several thousand people affected in Austria. Since the cardiac and lymphatic systems are in constant cooperation, it can only be assumed that if one system is disturbed, the other is also affected.However, limited knowledge is available on how lymphedema therapy affects cardiovascular responses. Therefore, the response of the cardiovascular system to the orthostatic changes will be examined.

Aims & Objectives: This study deals with the examination and measurement of various vital parameters of patients with lymphedema, which will be collected, during a sit-to-stand test, before and after a manual lymphatic drainage. The aim of this thesis is investigate how complete decongestive lymphedema therapy, specifically manual lymphatic drainage influences hemodynamic responses?

Methods: A total of 11 male and female patients (57 ± 8 years old, 167.2 ± 8.3 cm tall, 91.0 ± 23.5 kg weight) with stage II lower extremity lymphedema were chosen for the study. Treatment of lymphedema was based on current standards and was performed at the center of lymphatic disorders, Wolfsberg. It consisted of manual lymphatic drainage for 30 minutes, followed by application of compression bandages. Hemodynamic responses were recorded during a sit-to-stand test, before and after lymphatic drainage over several timepoints over three weeks of therapy. Heart rate, cardiac ejection rate, stroke volume and blood pressure were measured by electrocardiography, plethysmography and impendance cardiography. This thesis only deals with the collected values of day 1 of the study.

Results: Most of the expected differences in the parameters were not statistically significant. There were recurrent trends toward significance in the values, but too little to be described as significant. Heart rate significantly changed in epoch 6 (from 94 to 86 beats per minute ($p<0,001$)), epoch 7 (from 92 to 85 bpm ($p=0,059$)), epoch 8 (from 93 to 83 bpm ($p=0,008$)), epoch 9 (from 90 to 84 bpm ($p=0,044$)) and over all epochs ($F_{(9,72)}=2,53$; $p=0,014$). Significance was also achieved in the epochs of the cardiac output ($F_{(9,18)}=4,32$; $p=0,004$).

Conclusions: The results showed that manual lymphatic drainage had an influence on hemodynamic responses. The main factors for the changed values could be the higher available volume in the circulatory system, as well as the reduced pressure in the tissue due to lymphedema.

1. Introduction

1.1 Physiology of the cardiovascular flow and system function

A functioning cardiovascular system is fundamental for life and the survival of the human body. No other organ of the human body can compare to the precision and efficiency with which heart, vessel system and blood provide for every single cell. The main task is to guarantee a supply of oxygen (O_2) and nutrient substrates, as well as a disposal of waste products like carbon dioxide (CO_2) for every tissue. Apart from this supply, intercellular communication with hormones and temperature regulation through circulation of the skin are big tasks of the cardiovascular system. The mechanism with which blood is transported through the vessels of our body is very complex and adaptive to our environment or rather to the current situation of the body. Controlled by hormones and the autonomic nervous system, the cardiovascular system provides an optimal blood flow in and to every part of the body. (1)

1.1.a The way of the blood

The cardiovascular system begins at the most important part: the heart. The heart is a muscular, hollow organ in the shape of a cone. It lies in the middle of the thorax, between the two lungs, in the so-called mediastinum. (2) It has the same size comparable to the fist of the person and has to pump about 7000 liters through the body per day. The four chambered heart (two atriums and two chambers or ventricles) is divided in two parts: the right side and the left side. The chambers and atriums on each side are divided by the atrioventricular valves - the tricuspid and mitral valve. There are valves at the beginning of the outgoing arteries (pulmonary and aortic valve) which prevent the blood from flowing in the wrong direction. (2)
The cardiac circle has two phases: The diastole and systole. During the diastole, which is the heart refilling phase in the cardiac circle, the atriums and ventricles fill up with blood. In the following, systole phase the muscle cells of the heart, the myocardium, contract and pump the blood out.
The right side of the heart collects the deoxygenated blood from the body system and transports it into the lungs, where it is re-oxygenated again and loses its carbon dioxide. Blood from the upper part of the body arrives through the vena cava superior in the right atrium, where it blends with the blood from the vena cava inferior, which was collected from the lower parts of the body. During the systole the blood leaves the right chamber through the pulmonal valve and gets into the pulmonary arteries which lead directly into the lungs. (2)

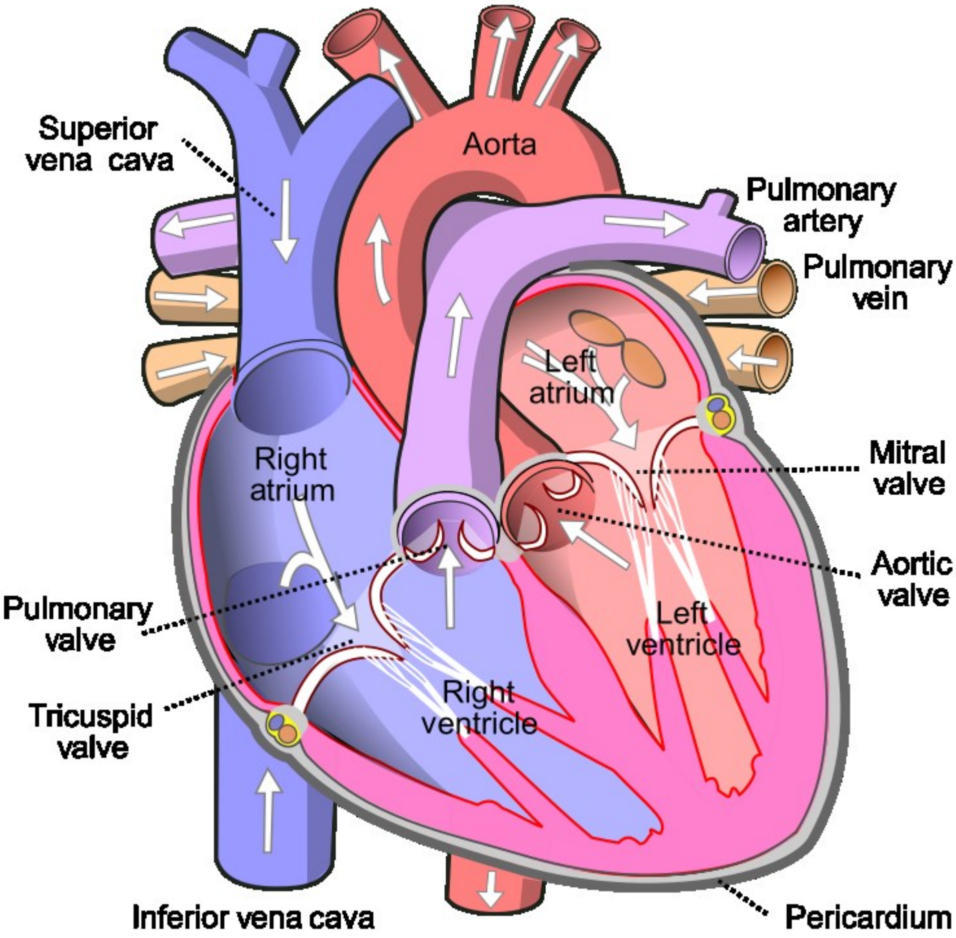

Figure 1. shows the anatomy of the heart. Taken from: (https://en.wikipedia.org/wiki/Circulatory_system#/media/File:Diagram_of_the_human_heart_(cropped).svg)

In the lungs, the deoxygenated blood is refilled with oxygen by freshly inhaled air and loses its carbon dioxide to the exhaled air. After this refilling, the blood flows back into the left atrium of the heart in the pulmonary veins. After passing the mitral valve during the diastole, the oxygenated blood comes into the left chamber and is pumped out again during the systole. Flowing through the open aortic valve into the aorta, the blood gets dispersed into every part of our body - even into the heart itself. (3)
The first vessels of the aorta are the coronary vessels. They are the heart's "private supply". The next outgoing arteries support the brain and upper parts of the body. On the way to the abdomen with all its organs and the lower extremities, the aorta is called the descending aorta and supplies everything with oxygenated blood through outgoing vessels or arteries. (3)

The vessels of the arterial system are becoming smaller and thinner as they reach the periphery of the body. At the size of 20-40 micrometers they are called arterioles. At their smallest size (about 5 to 10 micrometers) they turn into capillaries. There the vessels exchange nutrients and waste with the cells. Shortly after this point the vessels gain size again (up to 30 micrometers) and are defined as venules. They transport the “wasted“ blood back to the venous system where it is collected by the big veins and transported back to the right atrium. (3)

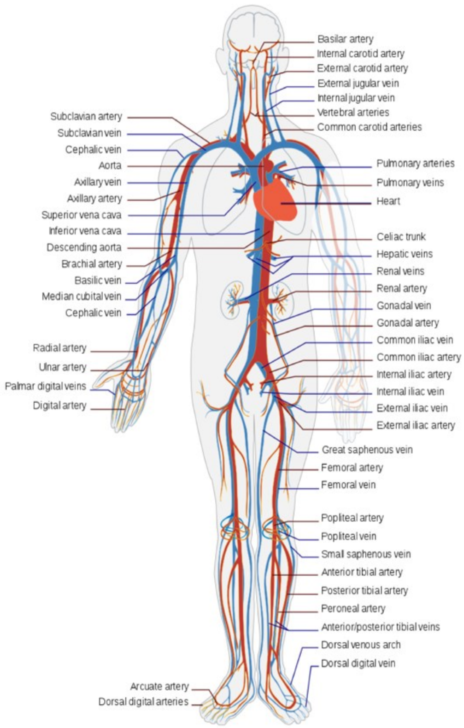

Figure 2. *shows the anatomy of the circulatory system. Taken from: (https://en.wikipedia.org/wiki/Circulatory_system#/media/File:Circulatory_System_en.svg)*

1.1.b The Blood

The main objectives of the blood are transport, signal transmission, heat preservation, preventing changes of the ph-scale, coordinating the immune defense and the coagulation system. The blood volume of an adult human body is about 7% of the lean body mass, which is about 4-5 liters in an average body. Most of the blood volume (about 80%) is contained in the venous system (because of its elasticity and capacity), the right heart and the lungs. (7)

The blood consists of the cellular part (haematokrit) suspended in the fluid part (plasma). The haematokrit - about 45% of the blood - is made out of 10^{12}/l erythrocytes, 10^{9}/l leukocytes and 10^{9}/l thrombocytes. The amount of

cells influences the viscosity of the blood and through that the flow resistance and capability to support the body with oxygen. (1)
The blood plasma consists of 90% water and 10% suspended substances. Most of the substances in the plasma are blood proteins - whereas the rest is made out of vitamins, gases, electrolytes, nutrients and metabolic products. There are more than hundreds of different plasma proteins like α_1/α_2 - globulins, β - globulins, C-reactive proteins and γ - globulins. But the most important protein is albumin. Because of its high concentration of 45 g/l plasma and its low molecular mass of 66 kDa, albumin plays a big role in the maintenance of colloid-osmotic pressure of the blood plasma. This pressure works against the hydrostatic pressure and ensures the retention of fluid in the cardiovascular system. (1)

1.1.c Cardiac conduction system

The heart has to pump blood through the vessels. For that, the muscle cells of the heart (also called myocard) have to contract and eject the blood. One of the special things of the heart is, that the excitation of the myocard is autonomous. It has its own conduction system consisting of nerve cells. The initial point of the contraction is the sinoatrial node - located in the right atrium at the end of the vena cava superior. It is the main pacemaker and sets the heart rate. From there the electric stimulus spreads out over both atriums and gathers at the atrioventricular node - found at the bottom of the right atrium, at the atrioventricular septum. From there it travels to the bundle of branches in the ventricles. In the ventricles the signal is transported by purkinje fibers to the myocard of the chambers. Along the way of the stimulus, the muscle cells of the heart contract. That causes a heart rate of an average adult of about 70 beats per minute (bpm) at rest. In, for example, stressful situations or during exercise, it can raise up to 180-200 bpm. As mentioned before, the sinoatrial node is the main pacemaker, with a depolarization impulse of 60-100 impulses per minute. On its way to the tip of the heart, the impulse frequency drops. At the atrioventricular node it has already decreased to at 40-55 impulses per minute. It is a kind of a frequency filter, in order to protect the heart ventricles from too high impulse frequency and to assure enough time to allow the chambers to fill with blood during the diastole. If the sinoatrial node fails, the atrioventricular node can take over its function as pacemaker. All of these electric activities can be measured by the electrocardiography (ECG). (1, 7, 29)

1.1.d Regulation of the circulatory system

Like mentioned above, the heart adapts its work to the current metabolism. The necessary factor here is the cardiac output, which is the blood volume pumped out of the heart per unit of time (l/min). In rest, the cardiac output of an average human is about 4,5-6 l/min. This amount depends on body size and body surface and is called the cardiac index (CI) ($CI = BV / min / m^2$). The regulation of the CI is caused by the change of the stroke volume (SV) and the heart rate (HR). These two can be regulated by two mechanisms: the sympathetic tone and the Frank-Starling-mechanism. (1)

The F-S mechanism describes that the force of the contraction is directly proportional to the preload of the heart. Which means that the heart's muscle cells are pumping more powerfully, the more they are stretched. With this mechanism the heart is able to support the body with a constant or higher cardiac output, at a higher preload or afterload. Moreover, it causes a precise adjustment of the pump-function of the right and left ventricle and prevents an accumulation of blood in the pulmonary circle. (1)

The sympathetic tone, however, is independent of the preload. It reacts to other factors like hormones or nerve receptors and causes a chronotropic (change of heart rate) and inotropic (strength of contraction) change. (1)

The main objectives of the body are to ensure a constant blood pressure and heart function. It controls this regulation through different mechanisms like O2-deficiency, metabolic waste products or vessel elongation, but the most important mechanisms are the hormonal and neuronal circulation controls. (2, 29)

The main hormones of the hormonal regulation are:

- **Nitrogen monoxide:** causes a paracrine vasodilation if acetylcolin, ATP, endothelin-1 or histamin binds to different receptors at the endothelial cells. (7)
- **Endothelin-1:** it causes a vasodilation by releasing nitrogen monoxide through ET_B-receptors or a vasoconstriction through ET_A-receptors if (for example) angiotensin II or vasopressin/ADH binds at the endothelial cells of the vessels. (7)
- **Adrenalin:** causes a vasodilation of the vessels through the α_1-adrenoreceptors and a vasoconstriction of the skeletal striated muscles, liver and myocard with the β_2-adrenoreceptors. (7)
- **Eicosanoids:** substances from the eicosanoids like prostaglandin $F2\alpha$ and the thromboxane A_2 and B_2 cause a vasoconstriction,

whereas prostaglandin E_2 and I_2 have a vasodilatating effect on vessels. (7)

- **Bradykinin, kallidin, histamin**: are all vasodilators. (7)

The neuronal circulation control operates with the sympathetic nervous system. Noradrenalin is the postganglionic transmitter and causes a vasoconstriction through the α_1-adrenoreceptors. The counter effect steps in with the decrease of the sympathetic tone. The cardiovascular centre is located in the brain, in the medulla oblongata and the pons. Their information about the current blood circulation comes from chemoreceptors in the high-pressure system (in the aorta and A. carotis) and the low-pressure system (in the V. cava and the atriums of the heart). They measure the arterial blood pressure, the fill pressure of the low-pressure system (= the blood volume) and heart rate. If any of these measurements show a change, the cardiovascular center reacts with impulses to the responsible body part. That system also contains a “pressing“ area, from which neurons send continuous sympathetic impulses to the heart and vessels. Connected by the vagus cores there is also a “depressing“ area, which lowers the heart rate, and the speed of the excitation in the conduction system. The heart beats autonomously, but it still needs commands from the cardiovascular center like the commands to change the heart rate, the force of the contraction and the speed of the excitation in the conduction system or the relaxation. These changes are caused by acetylcholin (lowers the heart rate) from the parasympathetic fibers of the N. vagus, noradrenalin from the sympathetic fibers of the N. vagus and adrenalin from the kidneys (both raise heart rate and the force of contraction). Other factors like the temperature or actions of the skeletal muscles also have an impact on the regulation, but to explain this in more detail would go beyond the scope here. (7)

1.2 Anatomy and physiology of the lymphatic flow and vascular system

For most people rather unknown and for some parts a not fully understood system of our body is the lymphatic system. It consists of the primary (bone marrow and thymus) and secondary (lymphatic nodes, spleen and tonsils) lymphatic organs. Its vessel system is spread over our whole body (except the central nerve system, bone marrow and the cartilage tissue) (5) and is almost as complex as the cardiovascular system. The system's function is to transport the interstitial fluid from the peripheral tissues and cells to the venous system. This fluid, called lymph, contains nutrients and waste products from the capillary, lymphocytes and other immune cells, as well as lipids from our food. That is why the functioning of our lymphatic system plays a big role in the support and protection of our body as the immune defense would be completely useless without it and a single cold could kill us then. (2, 4, 32)

1.2.a The anatomy

In contrast to the cardiovascular system the lymphatic system does not have a central muscle or pump which contracts to transport the lymph through our lymph vessels. Seen closely, it is also not really a closed circle like the blood system. The "journey" of the lymph begins in the periphery, at the capillary system - just at the change from arterial to venous blood. There, the blood is filtrated through the vessel wall. Because of the difference between the higher blood pressure (pushes fluid out) and the lower colloid osmotic pressure (pulls fluid back), just 10% of the fluid stays in the interstitium. About 2-3 liters of interstitial fluid is produced per day (2, 32).

There it flows between the cells, until it reaches the blind beginning lymph capillary - called the vasa lymphatica initialia. Now the fluid is called lymph. From there, the lymph flows into the larger pre-collector to collector vessels. The collector vessels lead to the big trunci lymphatici. (2, 8)

These trunci lymphatici divide the whole body in four quadrants. The lower influx area of the lymph is collected by the truncus intestinalis (single organs like spleen and digestive tract) and the truncus lumbalis sinister/dexter (lower extremities, pelvic and its organs and all the paired abdominal organs). These two trunci unite at the so-called cisterna chyli at the height of the 1-2 lumbar vertebrae. (2)

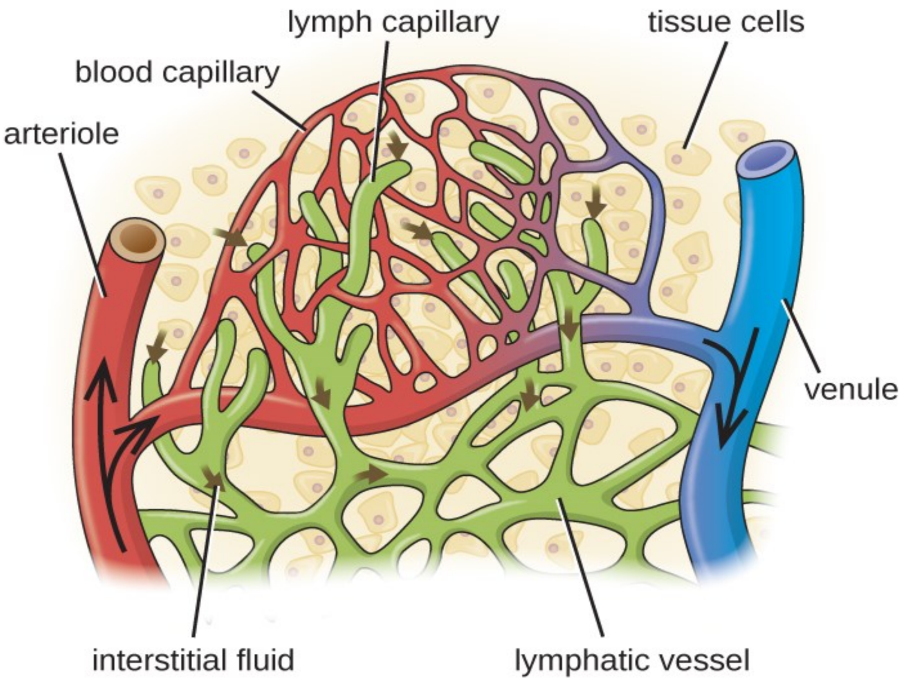

Figure 3. *shows the filtration of interstitial fluid from the blood capillary system. Taken from: https://openstax.org/books/microbiology/pages/25-1-anatomy-of-the-circulatory-and-lymphatic-systems*

From there on the main trunk is called ductus thoracicus. This vessel is about 40 cm long and lies on the right side of the aorta. It passes through the diaphragm at the aortic hiatus and collects the lymph from the truncus bronchomediastinalis sinister (left side thorax organs) the truncus subclavius sinister (upper left extremity) and the truncus jugularis sinister (left side of the head and cervix). After that, the ductus thoracicus ends in the left venous angle, made by the left vena jugularis interna and left vena brachiocephalica. (3)
At the other side of the upper influx area the truncus bronchomediastinalis dexter, truncus subclavius dexter and truncus jugularis dexter unite in the ductus lymphaticus dexter, which leads into the right venous angle. (3)
Summarized - the ducus thoracicus collects all the lymph from the two lower and the upper left quadrants - whereas the ductus lymphaticus dexter collects all the fluid from the upper right quadrant. Which makes the anatomy of the lymphdrain not symmetric in our body. (2)

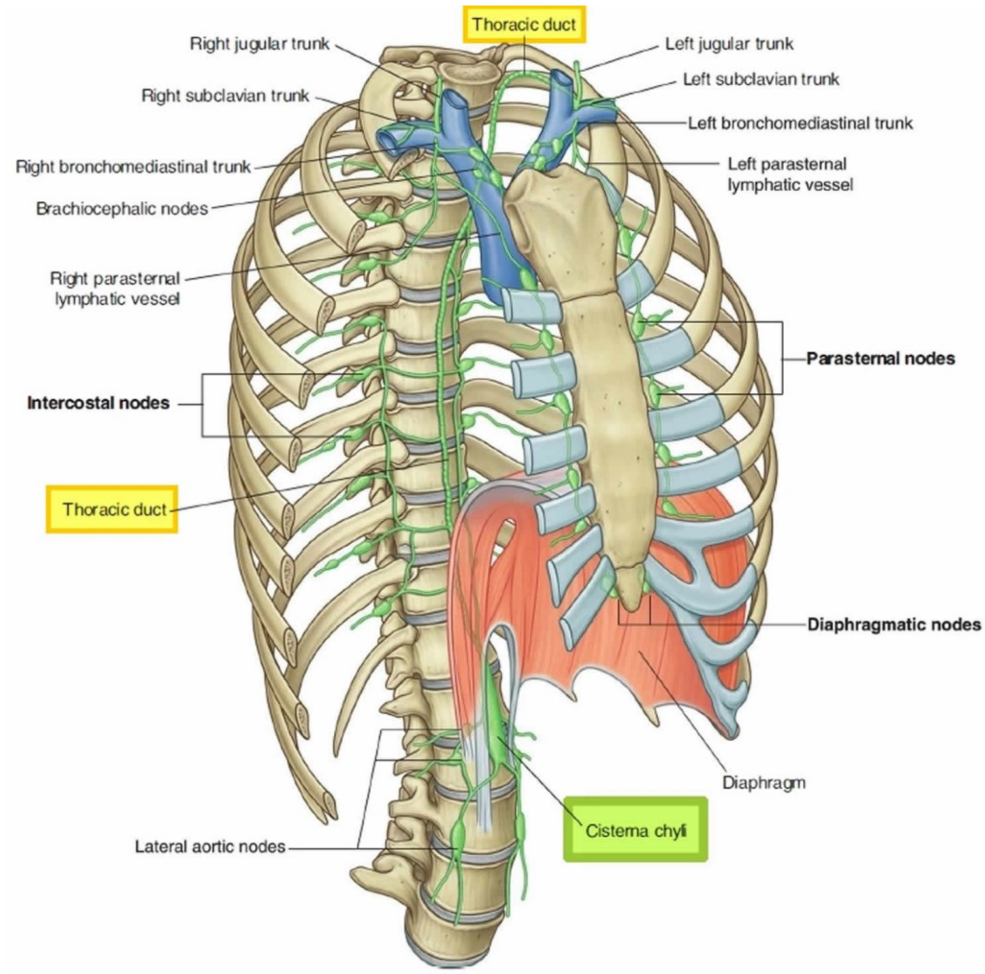

Figure 4. *Shows the anatomy of the lymphatic trunci. Taken from: https://healthjade.net/thoracic-duct/*

In general, the lymphatic system is divided in two systems: the vasa lymphatica superficialia and vasa lymphatica profounda. The superficial one is located above the body fascia and collects all the lymph from the skin and subcutis. The profound system lies beneath and collects the lymph of all organs, bones, muscles and nerves. Only the profound system has a connection with the trunci lymphatici. So, the superficial system has to break through the body fascia to connect with the other system. The connection between them is especially pronounced at three places in our body: At the groin, the armpit and at the lateral sides of the neck. (2, 3)
As mentioned before, the lymphatic system has no central muscle which pumps the fluid through the body. There are several mechanisms that help to transport the lymph. As you can see, the main lymphatic trunci are located near the big arterial vessels, like the aorta. The regular pulsation of the aorta increases the pressure on the lymph vessels and pushes the lymph forward. Also, the contraction of muscles, respiration, flaps and

intestinal peristalsis help the lymph to circulate. These mechanisms are called extrinsic pumping. Lymph can also be transported by intrinsic pumping, which is the rhythmic contraction of muscle cells in the vessel wall. Moreover, there are also valves in the lymphatic vessels, which prevent the lymph from flowing back. (6, 8)

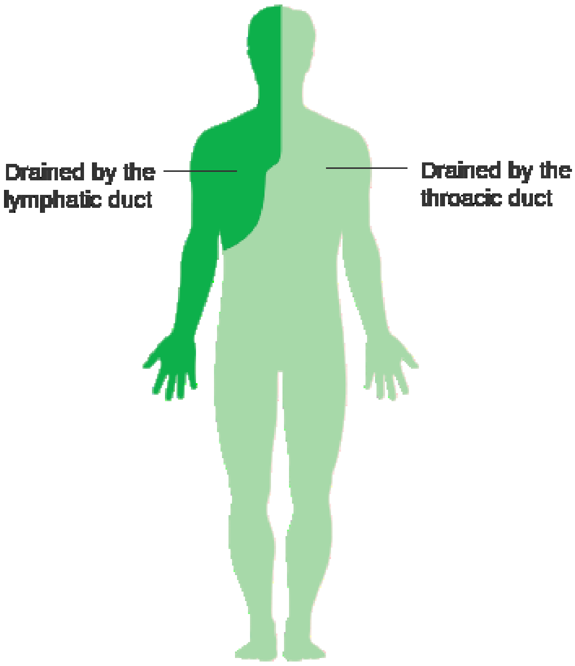

Figure 5. *shows the lymphatic quadrants. Taken from: https://en.wikipedia.org/wiki/File:Diagram_showing_the_parts_of_the_body_the_lymphatic_and_thoracic_ducts_drain_CRUK_323.svg*

On the way back to the venous system, the lymph has to pass several (about 600-700) antigen filtration stations - so called lymph nodes. These nodes are located along the whole lymphatic system. The most organs / body regions have specific lymph nodes, which are connected in series (primary, secondary and tertiary lymph nodes). This means, the nodes are not randomly located and the lymph has to undergo several filtrations, until it flows back to the blood system. (5, 8, 32)

The nodes are bean-shaped and about 1.5 cm long. The cover of the nodes is made of a capsule, which consists of muscle cells and collagen connective tissue. From the capsule, trabecula loom into the center of the node - so the node is stable. Because of this structure, the lymph is forced to flow slower in them than in the periphery. On the concave side there is the so-called hilum where the blood vessels enter and leave the node. The lymphatic vasa efferentia also leaves the node at the hilum. At the other, convex side, the vas afferens enters the node. (5, 8)

1.1.b Physiology

To fully understand the physiology of the lymphatic system, you have to take a close look at the beginning: the blood - or more precisely - the blood plasma. It is about 58% of the blood's volume and consists of 90% water and 10% suspended substances. Most of them are proteins - the most important ones are divided in 60% albumin and 40% α_1/α_2 - globulins, β - globulins and γ - globulins. There is also a small part of fibrinogen, C-reactive proteins, vitamins, gases, electrolytes, nutrients and metabolic products. These proteins play a big role in the blood buffering, the immune system, the maintenance of the colloid-osmotic pressure, the nutrition and the transport of other substances. (1, 8)

As mentioned in the section above, the exchange progress in the capillary system through diffusion, osmosis, reabsorption, filtration and migration of cells causes the development of the lymph. At the start of the capillary system, there is a blood pressure of 40 mmHg, but at the end, there is just 15 mmHg. The blood is filtrated with this pressure through the capillary vessel wall - while blood cells and most of the "bigger" molecules are retained. Small molecules like H_2O, O_2, CO_2 or NaCl can easily pass through, whereas bigger molecules like glucose or proteins have to stay. This higher concentration of proteins in the blood causes the colloid osmotic pressure to increase to about 25 mmHg and sucks 90% of the fluid back into the capillary system. Due to this and the resulting falling pressure, the re-uptake of the fluid decreases. Besides that, the amoeboidal-moving leukocytes move through the vessel wall into the space between the cells. (8, 32)

There this interstitial fluid, called interstitium, collects substances like proteins (for example during an inflammation), fat (collected by lymph vessels of the small intestine), self or nonself organic particles (erythrocytes during injuries, …), inorganic particles (carbon, silica, …) or cell waste products. Once the fluid is collected by the vasa lymphatica initialia it is called lymph. How much of these collected products the lymph has to carry, depends on different factors like temperature, physical exercise (more movement = higher temperature = metabolic increase) and food consumption (more water/fat = more lymph).(1, 8)

The transport of the lymph is supported by valves, the pulsation of the blood system, the movement of skeleton muscles and the suction effect during

breathing in the chest. Even the movement of the intestine influences the transport. All of these factors should be considered during a lymphatic drainage. (8)
The generally known lymph nodes have an important mission in our body. There are about 600-700 nodes embedded in fatty tissue in the lymphatic system. Because of their anatomy, the lymph has to flow 100 times slower inside them. By this, the immune system is able to send in the antigen presenting cells to the T-/B-cells (which are also developed there). Further, the nodes reduce the water of the lymph (about 50%). The nodes are not fully filled with lymph and cells. Only during an infection or lymph stasis the nodes are fully filled and palpable at some specific areas of the body. (8)

1.3 Lymphedema and current therapy

Right at the start: Lymphedema is not a disease; it has been a well-known symptom for hundreds of years. At the end of the 19th century the surgeon Prof. Ritter Alexander from Winiwarter recommended to elevate and compress the affected extremity. In the following years the therapy was improved and optimized, so the results also became better. Nowadays it affects about a few thousand people in Austria and is therefore a symptom every doctor be aware of. (8, 9, 24)

1.3a Symptoms and causes / Pathophysiology

The definition of lymphedema is an unphysiological storage of fluid in the interstitial or extravascular space. There are also some synonyms like hydrops (fluid in preformed visceral cavities), anasarka (expanded fluid between the tissue of the skin) or elephantiasis (extreme chronically lymphedema in the legs). Terms like myxedema or lipedema should be differentiated from the lymphedema, because they are not lymphedema per se. (8, 30)
The etiology of lymphedema is complex and there is not always “just one“ thing “wrong“. But because of their etiology, lymphedema are divided in two types: the idiopathic or primary lymphedema and the secondary lymphedema. In the primary group, most of the time a dysplasia of the lymphsystem is the main cause. The second lymphedema is the consequence of another disease. In Europe the main reason for secondary lymphedema is the consequence of an invasive cancer therapy, like surgically extraction of lymphnodes. (8, 9)

Lymphedema accrue from the disparity of filtration, reabsorption and lymphdrain. If, for example, the filtration is too strong, like during an inflammation, the tissue collects too much blood fluid. The lack of blood plasma proteins or the unphysiologically high amounts of proteins in the lymph (like albumin) can also cause a reabsorption which is too weak to collect all the fluid in the interstitium. Based on the insufficiency of the lymphatic system, there are three different types:

- **The dynamic insufficiency** (lymphatic system is healthy, but it is pushed to its limits)
- **The lymphostatic insufficiency** (the lymphatic system is unable to transport the fluid and proteins)
- **The combined insufficiency** (chronic insufficiency of the lymphatic system in combination with another edema causing problem) (8)

It is always important for the following therapy to know if the fluid of the lymph is full of proteins or not. Many proteins in the lymph can cause fibrosis and adherence between the tissues, which influences the lymphatic drainage therapy. Lymphedema, because of a lymphostatic insufficiency, are low in proteins, whereas the lymph of chronic edema are rich in proteins. (8, 30)
The diagnosis of lymphedema is actually pretty simple. Inspection and palpation of the affected area is sufficient. Asymmetric occurrence could be indicative for a local problem, whereas a symmetric deformation is more likely combined with a systemic problem. The patient often reports a feeling of tension, heaviness and pressure. Pain and restriction of movement are rare symptoms. Lymphedema can be classified in four different stages:

- **Stage 0** - No swelling or palpable edema.
- **Stage I** - spontaneously reversible edema
- **Stage II** - not spontaneously reversible edema
- **Stage III** - Elephantiasis (8)

Figure 6. *shows the different stages of lymphatic edema on the lower extremities. Taken from: https://upload.wikimedia.org/wikipedia/commons/thumb/1/1f/Lower_Limb_Lymphedema.png/588px-Lower_Limb_Lymphedema.png*

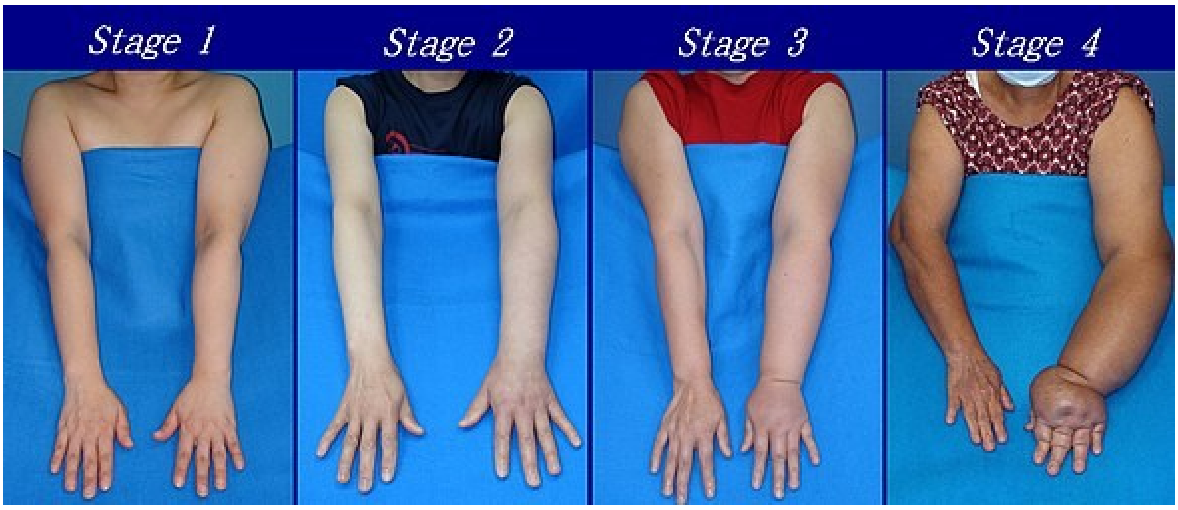

Figure 7. *shows the different stages of lymphatic edema on the upper extremities. Taken from: https://upload.wikimedia.org/wikipedia/commons/thumb/2/21/Upper_limb_lymphedema.jpg/588px-Upper_limb_lymphedema.jpg*

1.3b Physical decongestive therapy / lymphatic drainage

As mentioned before, decongestive lymph therapy has been known for a very long time. 1892 a surgeon recommended to treat lymphedema with massages and compresses. There are several different options to treat the patient. From intermittent compression to surgical treatment, there is a wide range of possibilities. (8, 9)

One of the most important treatments is the manual lymph drainage. It is a special type of massage, with focus on the anatomy and physiology of the lymph system. Circular stretching and shifting technique are used here in order to affect the skin and subcutaneous areas. The aim of the therapy is to strengthen the lymph vessel activity and therefore cause a positive effect on the lymphatic drainage. A pain relieving, a vagotonous (like sleep-inducing) and sympathicolytic (like heart rate reducing) effect can be observed, too. Just a few contraindications limit this therapy: malignant tumors, acute infections, heart failure, cardiac arrhythmia or venous thrombosis. (8, 9, 24)

Another common therapy is the compression with bandages, stockings or a machine. When rising the pressure in the tissue, the fluid is distributed, and the filtration of the blood vessels is reduced. That causes a better reabsorption of the fluid into the blood capillary system. There are several different techniques and materials to apply the compression, adapted to the problems of the patient. This therapy can be used to reduce lymphatic edema, pregnancy edema, venous edema or lip edema. Contraindications of this therapy are acute infections, heart failure, poor general condition or skin diseases at the compression's place. A so called complete decongestive therapy (CDT) is a combination of the compression with bandages and the manual lymph drainage. (8, 25, 28)

Latest studies indicate that these manual lymphatic drainages could have positive effects on the endothelial function of lymphedema patients. (26)

A classic lymph edema medication could be the application of diuretics. But they are not really used in the clinics, because they do not support the therapy. (9)

At last, the surgical treatment of lymph edema is also an option. It should increase the lymphatic transport capacity and reduce the lymphatic load, in order to stabilize the balance between them. Sadly, there are a great number of operative procedures, but no single method could be regarded as a golden standard. (9, 27)

1.4 Orthostatic challenge and cardiovascular responses

As stated above, the main goals of the cardiovascular system are to ensure a constant blood flow in the body and to supply the currently most needed organs with nutrition. It is a simple task, but if the body changes its position in gravity, a complex mechanism prevents us from a collapse or a so called “blackout“. From, standing up from bed in the morning (32), to weightlessness in outer space (34), our body has to respond to the blood shift (32).

In every blood vessel of our body there is a so-called hydrodynamic pressure. It occurs as a result of the pressure caused by blood in the vessels, called mean filling pressure, and the pumping-pressure of the heart and its counteracting blood flow resistance. If the body changes its position, gravity influences the fluid and additionally causes hydrostatic pressure. The region of our body, where the pressure does not change, no matter which movement or position, is called the hydrostatic zone of indifference and is located just below the diaphragm. If the body changes its position from horizontal “lying down“ to vertical “standing up“, blood rushes into the legs because of gravity and the vessels above the zone of indifference loses pressure, whereas the vessels under this zone, gain pressure. (1, 34)

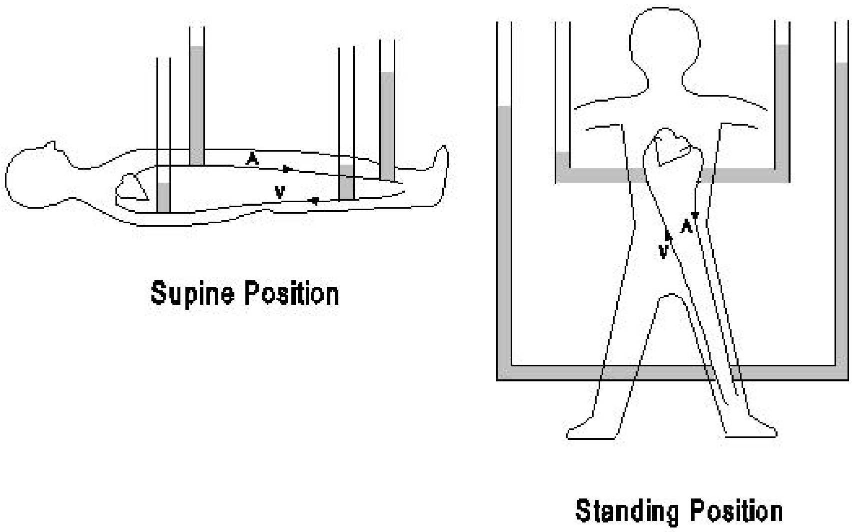

Figure 8. *shows the effect of gravity on cardiovascular pressures. Taken from: http://www.columbia.edu/~kj3/Figures/Figure3-4.jpg*

Standing up causes a loss of the preload of the heart. The Frank-Starling mechanism reacts immediately: the sympathetic tone increases and the vagal tone decreases. This leads to a release of norepinephrine which in turn increases the heart rate, the arterial constriction and the stroke volume is lowered. An abating of the excitation of the pressure receptors (baroreceptors), the lowering of oxygen partial pressure (P_{O2}) as well as the increase of carbon dioxide partial pressure (P_{CO2}) cause a reactive rise of the blood pressure. Due to the rising concentration of the hormone aldosterone in the blood, the glomerular filtration rate (GFR) is reduced and leads to a sodium and water retention. This mechanism causes a slow rise in blood volume and mean arterial pressure. (10, 34)
The peripheral resistance mainly rises in the muscles, skin and the abdominal blood vessels. The mean arterial pressure rises slightly, because the main arterial baroreceptors are located above the diaphragm. An increased diastolic pressure and afterload also help to reduce the stroke volume. (1)
Because of the different elasticity and volume capacity of the arterial and venous system, a big shift of volume in the veins occurs. When the body straightens up, about 500 ml blood flow into the legs and raise the hydrostatic pressure. At the same time, the chest releases its blood to fill the legs, especially (because of its elasticity) the blood from the lungs. (1)
In daily life, a lot more muscles are activated during a position change. Even when we stand, the contraction of the muscles of the legs, compresses the veins and supports the transport of the venous blood back to the heart. That is why the venous backflow to the heart and the volume distribution of the vessel system is responsible for the level of stress the change of position causes for our cardiovascular system. Factors like the tone of the veins or ambient temperature can influence these systems (e.g., men fainting while standing upright for a longer time during a military parade). It should also be mentioned, that despite the rise of the hydrostatic pressure in the legs, a healthy person does not get any lymph edema. Because of the contraction of muscles, the arterioles, the capillary vessel pressure does not rise that much. In combination with the muscles pumping of the extremities, the filtration of the blood fluid is still constant. (1, 34)

2. Aims and Objectives

The physiology of the cardiovascular and lymphatic system has been researched and known for many years (32). Also, the treatment of lymphedema and their consequences for the patients' well-being have been researched (28). But there is no information to be found in the literature on how a complete decongestive lymphedema therapy alters the two systems mentioned above.
My thesis is based on a study which carried out different tests on patients with lymphedema. Tests were conducted before and after a lymphatic drainage over three weeks. The aim of the study was to search for changes in the lymphatic flow, cardiovascular function, cerebral blood flow, hormonal system, blood coagulation, blood pressure and orthostatic regulation.
In my thesis I will just concentrate on the hemodynamic response (heart rate, stroke volume, blood pressure, cerebral blood flow, blood flow in the lower limbs and the musculo-skeletal activity) during a sit to stand test, before and after the decongestive therapy, on the first day of the treatment.

Hypothesis: The CDT influences the cardio-postural interaction by rising the blood volume and has an impact on the related mechanisms for compensation.

3. Methodology

3.1 Ethical approval

The study was performed at the center for physical medicine and rehabilitation in Wolfsberg. The study was approved by the ethics committee of Klagenfurt Klagenfurt (A 03/17) and the Ethics Committee of the Medical University Graz, Austria (29-090 ex 16/17). The experiments all followed the rules and regulations stated in the good clinical practices and the latest version of the WMA Declaration of Helsinki (2013). Each participant was informed in detail and gave written and informed consent before participating.

3.2 Patient selection and study design

In total 11 male and female patients (57 ± 8 years old, 167.2 ± 8.3 cm height, 91.0 ± 23.5 kg weight) agreed to participate in this study. Enrolling patients into this study followed strict inclusion and exclusion criteria. Patients with stage II lower limb lymphedema were included, whereas patients with signs of mental disorders, with histories of cardiovascular diseases, alcoholism or syncope and those on specific medications that influence the measured parameters such as beta blockers or diuretics, were excluded. Pregnant patients were also not included in the study.

The treatment of the lymphedema was based on the current standards and is routinely applied at the center of lymphatic disorders, Wolfsberg (21). It consisted of a daily manual lymph drainage for 30 minutes, followed by an application of compression bandages, which are worn by the patients until the next therapy session. Additionally, physical exercises (as e.g. walking and/or ergometry) are performed.

3.3 Measurement of hemodynamic responses

The required measurements were taken in a darkened, quiet room between 08:00 am and 12:30 pm. The temperature and humidity stayed at a constant level; 22-25°Celsius and 50 - 55% humidity. In order to receive a time-course of the effects, treatment was performed on day 1, day 2, day 7, day 14 and day 21. The data presented here were only taken from day 1 of CDT, directly before treatment and 30 minutes after lymphatic drainage.

3.3.a Assessment of the hemodynamic response

A sit-to-stand test was conducted in order to assess the hemodynamic parameters at rest and their responses to orthostatic loading. Hemodynamic parameters were continuously and non-invasively determined by a Task Force Monitor® (TFM) (CNSystems, Graz, Austria). In order to measure the blood pressure and heart rate, pressure cuffs were placed on the upper arm and on the fingers. Also, an electrocardiogram (ECG) was employed. The electrode stripes were placed in the neck and at the mid-clavicular line at the xiphoid process level for the transthoracic bioimpedance cardiography. During the tests the patients were first required to remain seated (baseline). Then they were asked to stand upright, holding their right arm at heart level with a sling. They were instructed to breathe normally and to focus their open eyes onto a certain spot on the wall in front of them.
During this procedure certain measurements were constantly taken by the TFM. These were:

- heart rate (by ECG)
- systolic blood pressure and diastolic blood pressure (by plethysmography)
- stroke volume (by transthoracic bioimpedance cardiography (ICG))

3.4. Data analysis and statistics

As previously reported hemodynamic data were analyzed using the MATLAB-Software (Version 2016b, The MathWorks Inc., USA.) From each phase of the sit to stand test, epochs of 10 second intervals (as shown in figure 9) were analyzed.

The acquired data were analyzed in the following epochs:

1) **last 10 seconds of baseline,**
2) **0-10 seconds standing upright**
3) **10-20 seconds standing upright**
4) **20-30 seconds standing upright**
5) **170-180 seconds (at 3 minutes) standing upright**
6) **150-260 seconds (at 5 minutes) of standing upright**
7) **0-10 seconds of recovery**
8) **10-20 seconds of recovery**
9) **20-30 seconds of recovery**
10) **last 10 seconds of recovery**

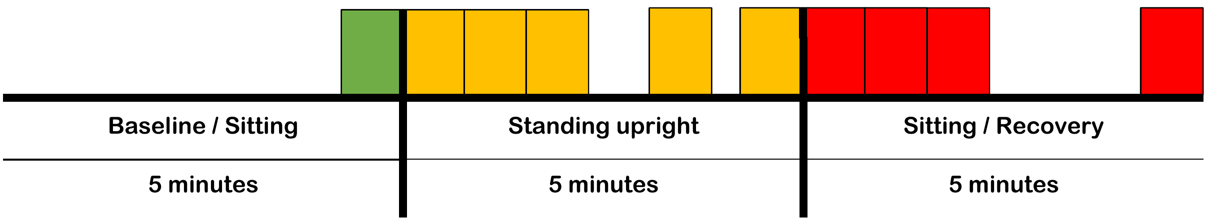

Figure 9. *shows the graphic display of the sit-to-stand test*

The hemodynamic responses of the body were analyzed by the two-way ANOVA for repeated measures with the following factors for each assessment day separately: epochs and pre-/post manual lymphatic drainage. SPSS statistics (Version 23, IBM, USA) was used for statistical analysis. P-values <0.05 were considered as statistically significant. The data are shown as mean ± standard deviation (SD). Figures show mean values ± standard error of the mean (SEM) for a better visualization.

4. Results

4.1 Heart rate

Heart rate showed an overall effect over all epochs during the sit-to-stand test ($F_{(9,72)}$=2,53; p=0,014). Epoch 4 and 10 tended to be different, however a significance was not achieved (p=0,073). Also, between epoch 5 and 10 a tendency to the difference is shown (p=0,073).

Comparing epochs before vs. post manual lymphatic drainage showed no significant difference, but tended to reduce post-MLD ($F_{(1,8)}$=4,74; p=0,061). Post-test showed a significant reduction pre/post-MLD for epoch 6 from 94 to 86 bpm (p<0,001), epoch 7 from 92 to 85 bpm (p=0,059), epoch 8 from 93 to 83 bpm (p=0,008) and epoch 9 from 90 to 84 bpm (p=0,044).
Also the interaction was not significant ($F_{(9,72)}$=1,20; p=0,310).

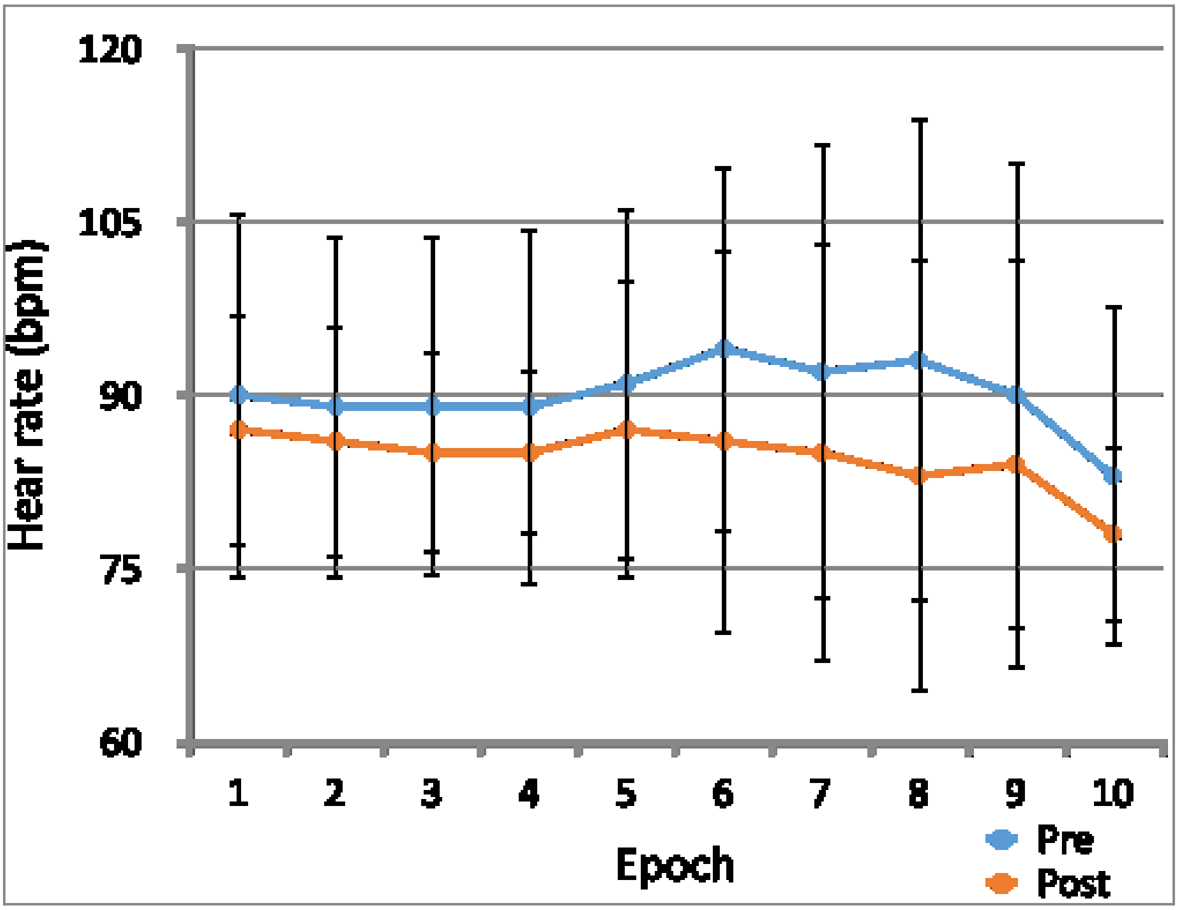

Figure 10. Heart rate pre - manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.2 Cardiac output

For the variable cardiac output a statistical difference was found in the epochs ($F_{(9,18)}$=4,32; p=0,004). Comparing the epochs with themselves – no significant difference was shown.

The comparison of the pre and post manual lymphatic drainage did not provide a significant difference ($F_{(1,2)}$=1,48; p=0,35). Overall, a downward trend was observed. The major difference occurred in epoch 5 (4,7 to 4,0 l/min; p=0,209), epoch 9 (4,7 to 3,9 l/min; p=0,059) and epoch 10 (4,5 to 3,7 l/min; p=0,235).
The interaction was not significant ($F_{(9,18)}$=0,32; p=1,00).

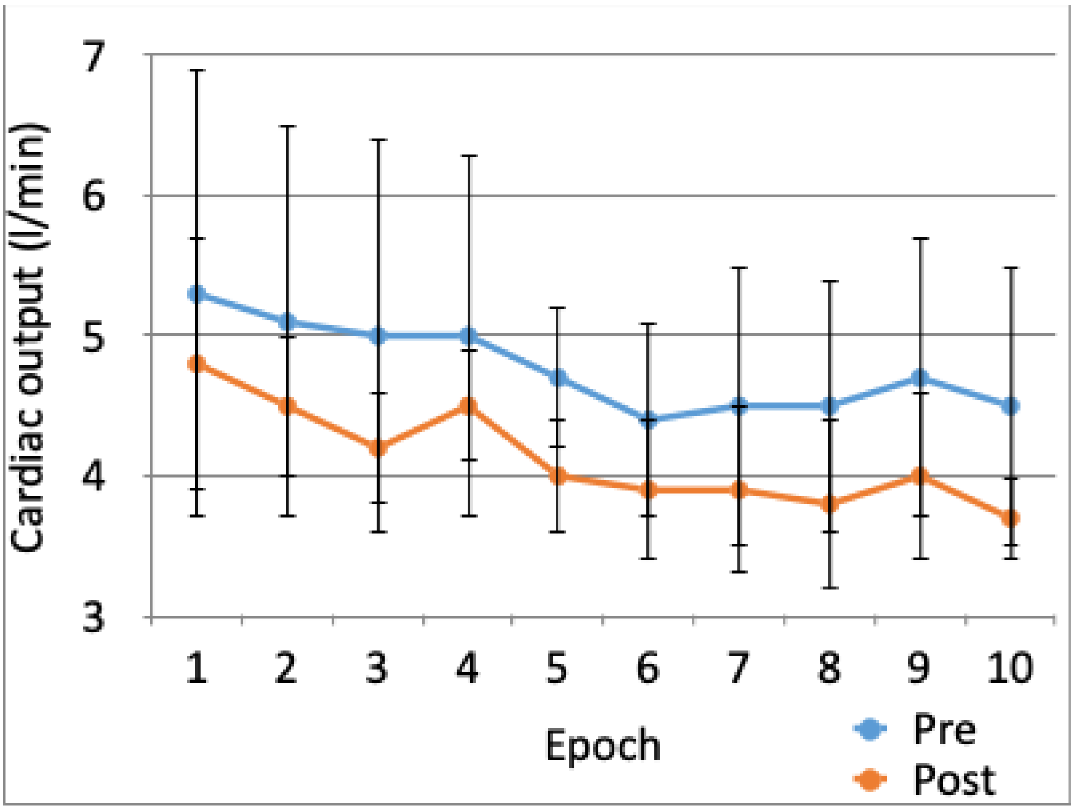

Figure 11. Cardiac output - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.3 Stroke volume

There was no considerable difference found in the epochs of the stroke volume (indicated in milliliters per stroke) during the sit-to-stand test ($F_{(9,18)}$=1,77; p=0,145). No significance was shown in any of the analysed epochs (p=1,000).

In the comparison of the epochs in the pre and post therapy no difference is shown either ($F_{(1,2)}$=1,77; p=0,314). Despite this, post-test showed an overall slightly downward trend, especially in epoch 4 from 57 to 52 (p=0,095), epoch 9 from 55 to 49 (p=0,184) and epoch 10 from 57 to 49 (p=0,161).
No significance was shown in the interaction either ($F_{(9,18)}$=1,13; p=0,388).

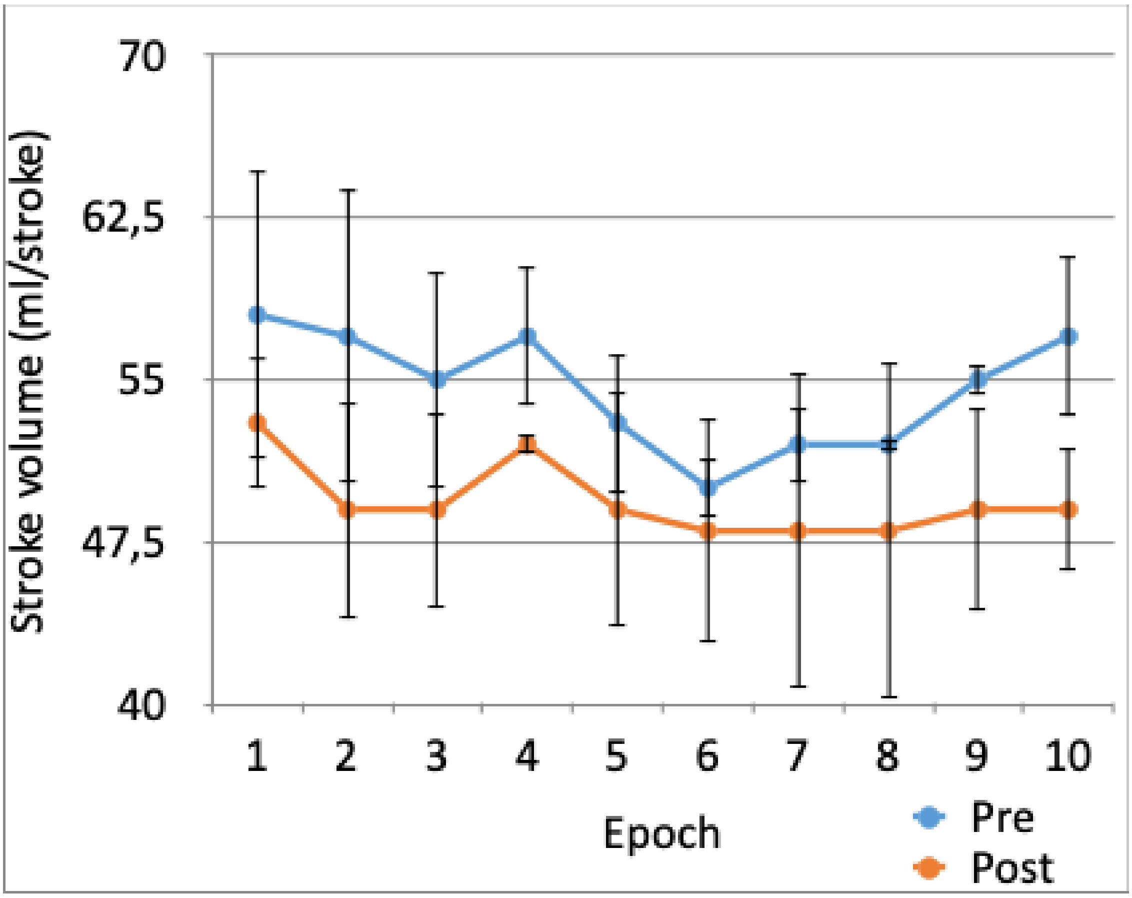

Figure 12. Stroke volume - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.4 Mean blood pressure

Orthostatic loading in form of a sit-to-stand test did not lead to changes in mean blood pressure over all epochs ($F_{(9,36)}$=0,43; p=0,909). Further, in the comparison of all individual the epochs pre/post MLD, no difference was shown (p=1,000)

No significant difference was found in all epochs pre- vs. post-therapy ($F_{(1,4)}$=0,44; p=0,54). Only between the following epochs there seems to be a tendency: epoch 1 (from 113 to 98 mmHg; p=0,186) and epoch 2 (from 113 to 100 mmHg; p=0,255). No significance is shown in the interaction ($F_{(9,36)}$=0,95; p=0,490).

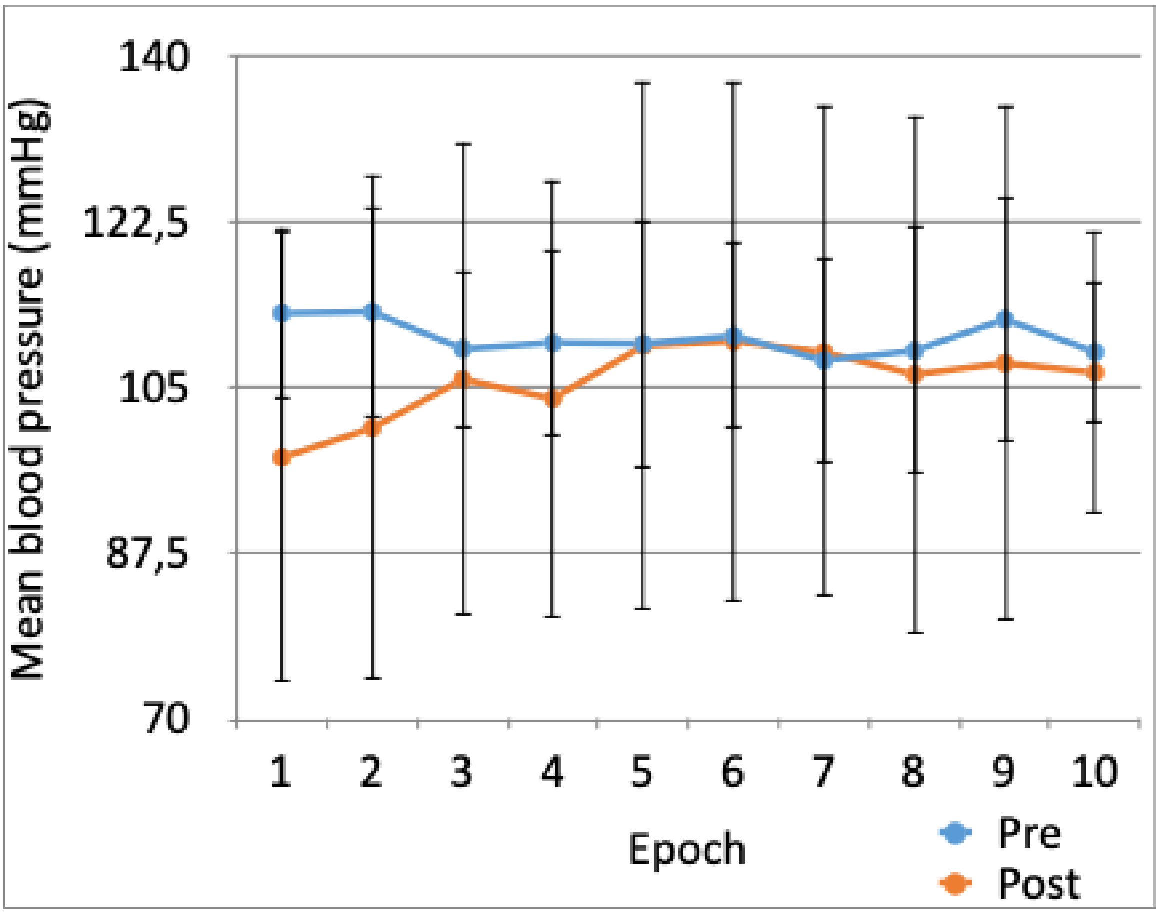

Figure 13. Mean blood pressure - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.5 Mean arterial pressure

The mean arterial pressure showed no significant difference over all episodes during the sit-to-stand test ($F_{(9,9)}$=1,29; p=0,355). Not even the comparison of all the episodes with themselves showed a tendency into the direction of a significant difference (p=1,000).

Comparing epochs during the before vs. post-MLD showed no significant difference ($F_{(1,1)}$=1,38; p=0,773). Post-tests showed a tendency in the reduction for epoch 1 from 91 to 64 mmHg (p=0,259). Also there was no significance in the interaction ($F_{(9,9)}$=2,79; p=0,71).

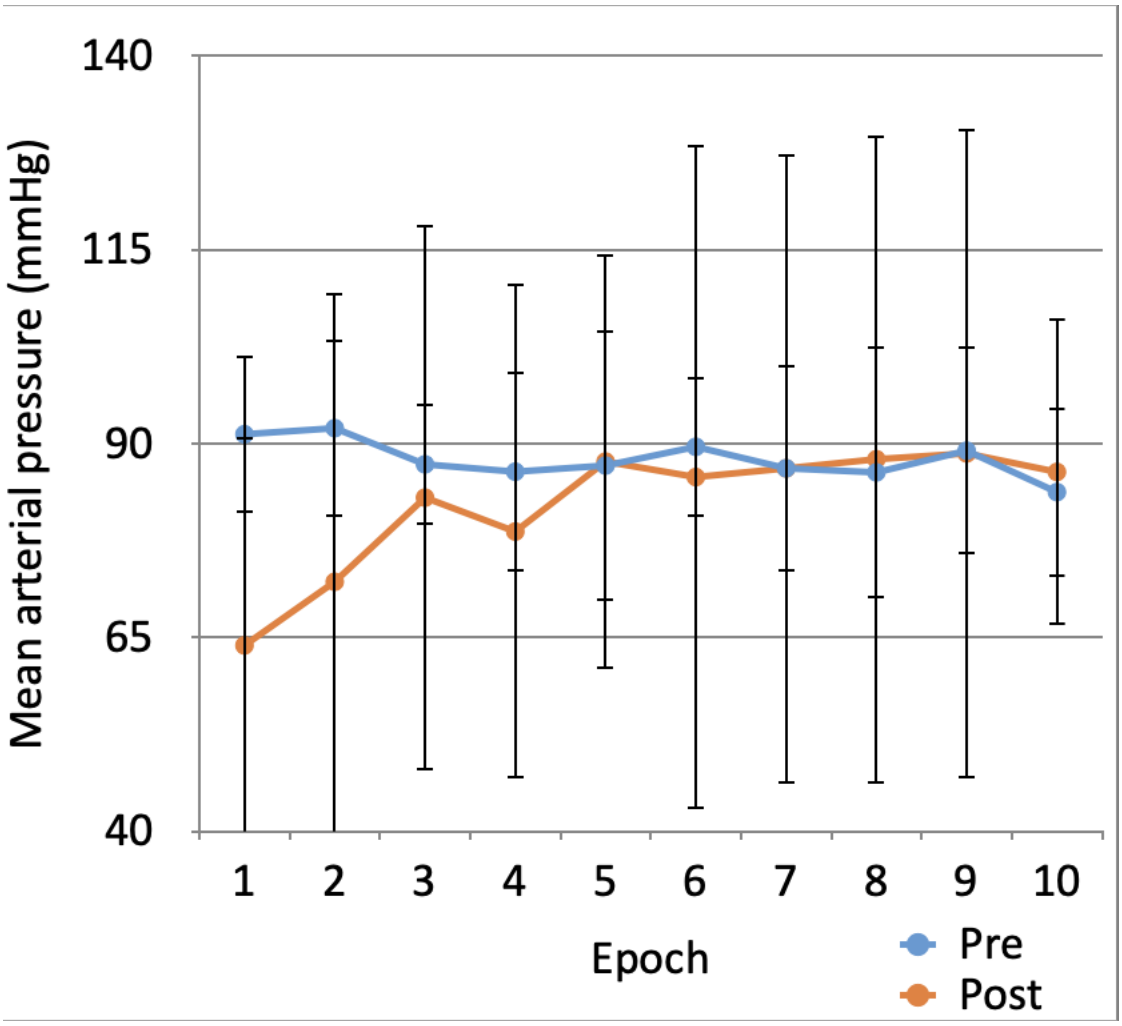

Figure 14. Mean arterial pressure - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.6 Systolic blood pressure

Concerning the variable systolic blood pressure no statistical difference was found in the epochs ($F_{(9,36)}$=0,30; p=0,969). Also, comparing the epochs with themselves – no significant difference was shown (p=1,000).

Comparing pre- and post-MLD of the pre and post manual lymphatic drainage, there was no difference shown ($F_{(1,4)}$=0,96; p=0,381). However, a downward trend was seen. The major difference occurred in epoch 1 (138 to 117 mmHg; p=0,105) and epoch 2 (139 to 120; p=0,131).
The interaction was not significant ($F_{(9,36)}$=1,59; p=1,56)

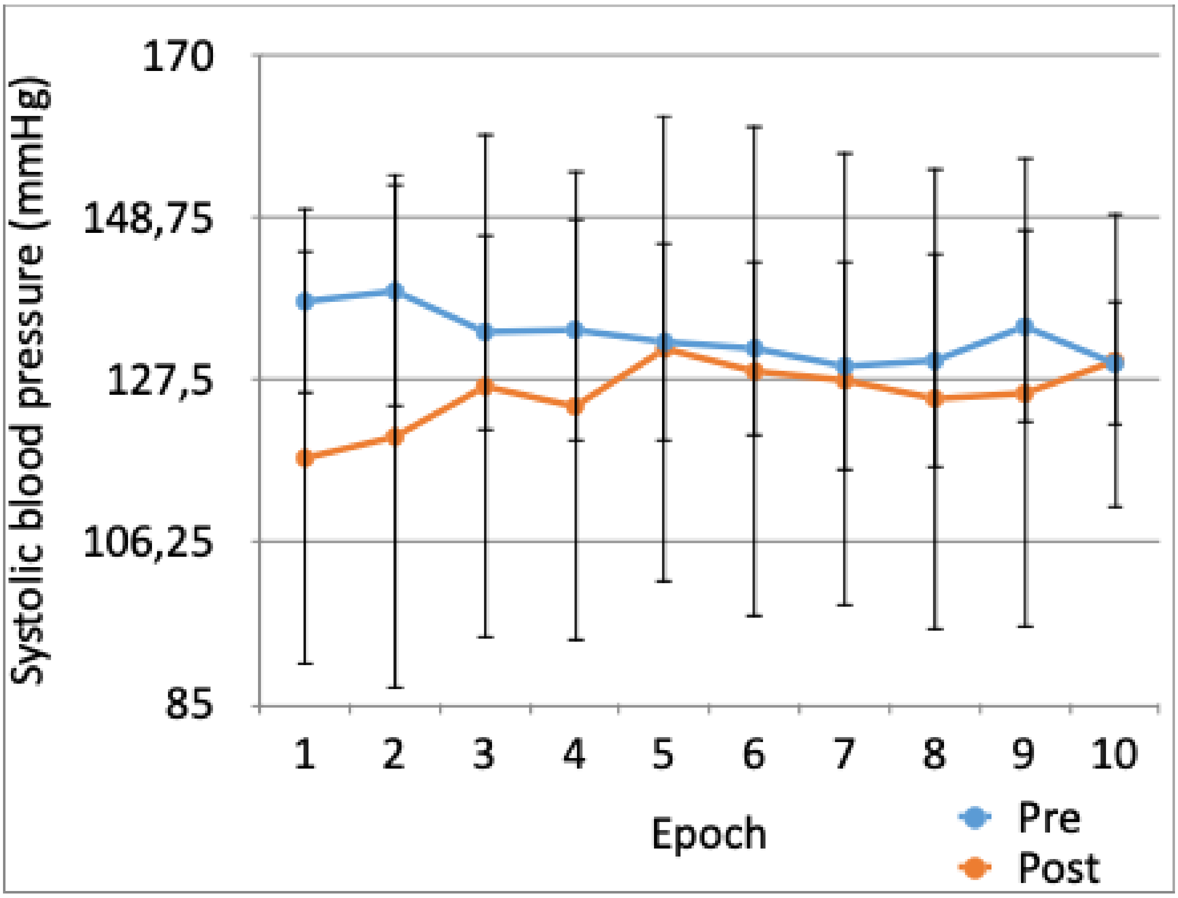

Figure 15. Systolic blood pressure - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

4.7 Diastolic blood pressure

No statistically significant difference were found in the epochs of the diastolic blood pressure during the sit-to-stand test $F_{(9,36)}$=0,715; p=0,692). Not even a single episode showed a significant difference or a tendency (p=1,000).

In the comparing of the epochs in the pre and post therapy, no significant difference is shown $F_{(1,4)}$=0,16; p=0,713). Only in the first epoch a tendency could be found (96 to 85 mmHg; p=0,338).
No significance was shown in the interaction ether ($F_{(9,36)}$=0,559; p=0,821).

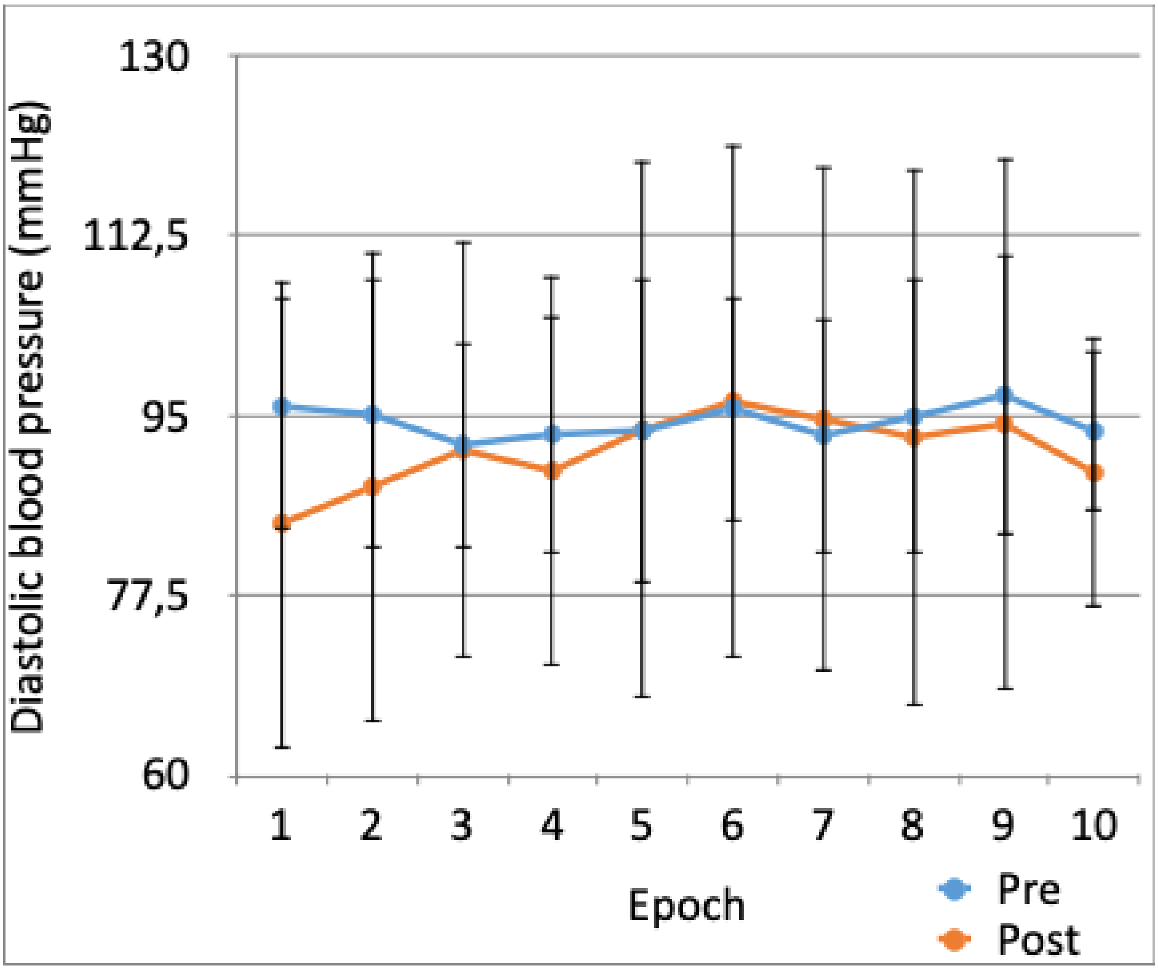

Figure 16. Systolic blood pressure - pre manual lymphatic drainage (MLD) epochs (blue line) compared with post-MLD epochs (orange line)

Table 1. shows the average value with the standard deviation of the pre- and post-MLD heart associated values.

		Epoch 1	Epoch 2	Epoch 3	Epoch 4	Epoch 5	Epoch 6	Epoch 7	Epoch 8	Epoch 9	Epoch 10
HR	Pre	90±15,8	89±14,8	89±14,7	89±15,4	91±15,2	94±15,8	92±19,7	93±20,9	90±20,2	83±14,7
	Post	87±10,0	86±10.0	85±8,7	85±7,1	87±12,9	86±16,6	85±18,1	83±18,7	84±17,7	78±7,6
CO	Pre	5±1.6	5±1,4	5±1,4	5±1,3	5±0,5	4±0,7	5±1,0	5±0,9	5±1,0	5±1,0
	Post	5±0,9	4±0,5	4±0,4	4±0,4	4±0,4	4±0,5	4±0,6	4±0,6	4±0,6	4±0,3
SV	Pre	58±6,7	57±6,8	55,9±5,0	57±3,2	53±3,2	50±1,4	52±1,7	52±0,22	55±0,7	57±3,7
	Post	53±3,0	49±5,0	49±4,5	52±0,4	49±5,4	48±5,2	48±7,3	48±7,8	49±4,7	49±2,8
mBP	Pre	113±9,0	113±11,1	109±8,3	110±9,9	110±13,1	110±9,9	108±10,8	109±13,1	112±12,9	109±7,4
	Post	98±23,8	101±26,6	106±24,9	104±23,1	109±27,9	110±27,4	109±25,9	106±27,3	108±27,2	107±15,0
MAP	Pre	91±10,2	92±11,5	87±7,9	86±12,9	87±17,5	90±9,0	87±13,3	86±16,2	89±13,4	84±10,9
	Post	64±26,8	72±37,3	83±35,2	79±31,9	88±26,7	86±42,8	87±40,6	88±41,8	89±41,9	86±19,8
sBP	Pre	138±12,2	139±15,3	134±12,9	134±14,6	132±13,0	132±11,6	129±13,7	130±14,0	134±12,8	130±8,1
	Post	117±27,1	120±32,9	127±33,0	124±30,7	132±30,5	129±32,1	127±29,7	125±30,3	126±30,7	130±19,4
dBP	Pre	96±12,1	95±13,1	92±10,0	93±11,5	94±14,8	96±10,9	93±11,4	95±13,3	97±13,7	93±7,7
	Post	85±22,0	88±22,9	92±20,2	90±18,9	94±26,1	96±25,0	95±24,5	93±26,1	94±25,8	89±13,2

5. Discussion

In this study, the impact of a single intervention of manual lymphatic drainage on the cardio-vascular system was investigated on the first day of complete decongestiver therapy. Significant changes in the heart rate were observed in epoch 6 (from 94 to 86 beats per minute ($p<0.001$)), epoch 7 (from 92 to 85 bpm ($p=0,059$)), epoch 8 (from 93 to 83 bpm ($p=0,008$)), epoch 9 (from 90 to 84 bpm ($p=0,044$)) and over all epochs ($F(9,72)=2,53$; $p=0,014$). Significance was also achieved in the epochs of the cardiac output ($F(9,18)=4,32$; $p=0,004$). A tendency of reduction? is shown in the other values (SV, mBP, MAP, sBP and dBP), however, significance was not achieved.
The function and cause of the reaction of the heart and the vessels during the orthostasis are well known and have been researched (1, 3, 4, 5, 7). Therefore, there also have been a number of different studies about the negative and dangerous consequences of the lack of orthostatic response (11, 12, 13, 14, 15, 16).

The results of the heart rate measurements before the MLD showed the expected and in literature already known numerical values (1). Because of standing up, blood shifts into the legs and causes a reduction of the venous return and cardiac pre-load. In order to maintain the mean arterial blood pressure, the heart rate increases due to the Frank Starlin mechanism - as seen in epoch 2-6 (16). The minimal decrease of the heart rate in the first 30s (90 to 89 bpm) indicates the time the body needs to react to the fluid shift. As seen while sitting, in the epochs 7-10 the heart rate drops again (92 to 83 bpm), because of the reverse effect of the back shift of the blood. Even though the measurements of the post-MLD heart rate showed no significant reduction, the overall heart rate, during the sit-to-stand test, dropped. The post-MLD values showed almost the same development as the pre-MLD. The generalized drop of the heart rate could be connected with the presence of more fluid in the blood system and therefore more pre-load (1). The findings here are similar to Esmer et al. – they also describe a decrease of the HR. A possible cause could be of accelerating of the systemic circulation of fluid, the reduction of the workload of the heart and the localization of the arm (closer to the heart) (22).

Overall, the heart rate is higher than the physiologically value – this could be connected to the lymphedema and their effect on the cardiovascular system (7).

Due to the Frank Starlin mechanism the heart responses to the transition from the sitting to the standing posture with an expected reduction of the cardiac output (5,3 to 4,4 l/min). Because of this mechanism the excitation of the arterial pressure receptors reduces, and the sympathetic tone rises (1). Therefore, the resistance in the peripheral vessels rises due vasoconstriction, as does the heart rate, in order to maintain the mean arterial pressure (16, 17). The lack of returning blood from the periphery blood system and the increase of the resistance causes the overall continuous decrease of the cardiac output, as seen in the results (5,3 to 4,4 l/min). Only when the patient is sitting down again, the output stabilizes again and rises after 30s (as seen in epoch 9 (4,4 to 4,7 l/min)). The seen overall reduction of the pre-MLD cardiac output to the post-MLD output, may be due to the increase of available fluid in the blood system. The values of the cardiac output have an overall similar course before as well as after the massage therapy and therefore show no significant difference. The findings here are similar to Brix et al. They described the fluid shift due to the physical therapy, with an increase of plasma volume and plasma protein concentrations in the blood (25).

The stroke volume of the heart follows the same rules during the sit-to-stand test, just as the cardiac output. Due to the fluid shift to the lower half of the body when standing up, the sympathetic tone rises and causes the heart rate to go up and the peripheral resistance, as well as the afterload, to fall. Because of the reduction of the “back flowing” venous blood to the heart, the heart has to lower the stroke volume (1, 17). As seen in the data, the values fall (57 to 50 ml/stroke), till the patient sits down again. During the resting phase, the stroke volume recovers and rises again (50 to 57 ml/stroke). The stroke volume data before and after the lymphatic drainage, showed a similar development, but the post-MLD data generally show lower values than the pre-MLD data. This phenomenon could be related to the fact, that the lymph massage raises the blood volume in the vessels and therefor the afterload. This causes the stroke volume in general to be lower than before, but does not change anything regarding the regulation system, which maintains the blood support in the body.

The mean blood pressure is one of the key parts the body wants to keep up during the orthostatic change, in order to supply the organs with blood. That is why the heart reacts to the change of volume with the rise of the heart rate and peripheral resistance (1, 18). As seen in the data, the values of the pre-MLD did not change much. The blood pressure falls a bit while standing (113 to 110 mmHg) but stabilizes itself again when reaching the sitting phase. In contrast to this, the post-MLD data already start at a much lower value (98 mmHg). The mean blood pressure after the treatment is lower, because of the higher volume in the circulating system (25). During the active standing phase in the experiment the blood pressure has to rise to almost the same pressure as the pre-MLD values. When the resting phase is reached, the mean blood pressure falls again (110 to 106 mmHg), because the pressure does not need to be that high to provide enough blood for upper body parts like the brain.

In order to keep up the blood flow in the organs during the orthostatic change, the mean arterial pressure plays an important role. It has to be kept high, otherwise it leads to the so-called “orthostatic syncope” and the person’s collapse (19). As seen in the results, the pre-MLD mean arterial pressure drops a little bit in the active standing phase (92 to 86 mmHg). That is due to the blood shift from the upper body part to the lower one. This redistribution causes a decrease of returning venous blood in the heart, a reduction of the stroke volume and a fall in the blood pressure (17). It takes some time for the body to react to this shift, but after 5 min of standing (epoch 6) the pressure has returned to the initial value. Because of another fluid shift, the pressure drops again after sitting down (90 to 86 mmHg) – regulated by the same mechanisms as mentioned before. The post-MLD mean arterial pressure behaves in a similar way as the pre-MLD pressure. The average initial value in epoch 1 is much lower than the average value before the drainage (91 to 64 mmHg). This could be connected with the reduction of the lymphedema and the mental and physical relaxation after the lymph drainage. There happens to be more available fluid in the cardiovascular system (25), but during the orthostatic change the body manages to keep the pressure at the same value as before the therapy. Regardless of the blood volume, the mean arterial pressure is kept the same. Therefore, the lymphatic drainage has no great impact on it.

The systolic blood pressure represents an important component in maintaining the circulation of blood in the body. It is well documented that it should not change much during an orthostatic change (1). As seen in the results, the values, before the drainage in epoch 1 (138 mmHg), start very high. According to literature these values are indicative for a hypertension

(7). This circumstance could be connected with the consequences of the lymphedema disease (20). During the standing phase the pressure drops continuously until the patient sits again (139 to 132 mmHg). During the third phase of the test – the systolic pressure rises again and stabilizes afterwards (129 to 134 to 130 mmHg). This is unusual, because it is expected that the value initially drops during the standing phase, but then rises to the primary value. The post-MLD systolic pressure starts (just as the mean arterial pressure) at a lower and more physiological value than the pre-MLD pressure (117 to 138 mmHg). This is probably due to the reduction of the lymphedema, as well as the mental and physical relaxation after the lymph drainage. The pressure rises during the standing phase (120 mmHg to 132 mmHg), until it reaches almost the same value as the pre-MLD pressure (epoch 5). After this point, the overall pressure is lower and reacts similar to the pre-MLD, ending the sit-to-stand test with the same value as before (130 mmHg). This circumstance could not be explained due to the higher blood volume after the massage, but due to the lymphatic drainage itself. The loss of all the edema with their pressure on the tissue could cause the overall drop of the systolic pressure. Even though there should be a generalized rise of the blood pressure, caused by the higher amount of fluid in the blood system (20). Esmer et al. also reported a decrease in systolic blood pressure after MLD (22). The results here show a similar effect. Possible influences for this cause, such as the parasympathetic effect of MLD and the fact that the participants were being placed in the supine position for a long time, were discussed.

It is known that due to the Frank Starling mechanism the fluid shift in the lower body parts and the higher afterload, the diastolic blood pressure should rise a little bit during an orthostatic change (23). The heart needs blood to supply the upright standing body with blood, so the “heart-filling-pressure” rises. As seen in the results, the average diastolic pre-MLD pressure starts at a value that could be related with hypertension (96 mmHg) (1, 7). This could be caused by the lymphatic edema of the patients. When the patients stand up, the pressure falls a bit (96 to 93 mmHg). After 5 min, it rises back to the initial value (96 mmHg). Back in the sitting phase, the pressure falls again (96 to 93 mmHg), but rises back quicker than before (93 to 97 mmHg). This could be explained because of the more favorable blood shift when sitting. After 5 minutes of sitting (epoch 10) the value drops again (97 to 93 mmHg). Also, the post-MLD diastolic pressure initially starts at a lower and more physiological value than the pre-MLD pressure (85 mmHg), supposably due to the reduction of the lymphedema, as well as the physical and mental relaxation after the lymph drainage. After standing upright, the pressure rises as expected (85 to 96 mmHg). It even exceeds the pre-MLD pressure value after 5 minutes of standing (96 mmHg in epoch 6). This could be explained by the higher volume in the vessel system (25). After reaching the sitting phase of the test, the values show a similar course as before the therapy.

6. Conclusion

This study indicates that manual lymphatic drainage therapy has an impact on hemodynamic response. However, significance was not always achieved, the therapy reduced all of the values associated with the heart. The main factors could be the higher available volume in the cardiac system and the reduction of the swelling caused by lymphedema and therefore a smaller impact on the affected tissue. The heart has to deal with more volume than before the massage – which could be compared with the reaction to an intravenous infusion. Interesting is the fact, that the average values of the patients before the drainage are associated with hypertension and stabilize to a more physiological level after the treatment. After all, the values show an expected course. However, my thesis only shows the impact of the lymphatic drainage on day one. The results of the whole study could be more significant and the work can serve as a basis for further studies in order to help to a better understanding of the underestimated consequences of the manual lymphatic drainage on the human body.

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