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DISSERTATION

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"Arterial stiffness and physical performance capacity in young male soccer players."

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“In extreme old age, the arteries themselves, the grand instrument of the circulation, by the continual apposition of earth, become hard, and as it were bony, till, having lost the power of contracting themselves they can no longer propel the blood, even through the largest channels, in consequence of which death naturally ensues.”

John Wesley, 1703 - 1791.
(In:Quinn et al. 2012)

Preface

Ich möchte meinen beiden Betreuern danken, dass sie mich bei meiner Dissertation unterstützt, mir mit Rat und Feedback weitergeholfen und mir in vielerlei Dinge das Durchführen meiner Studie ermöglicht haben. Besonders möchte ich ihnen dafür danken, dass sie mich weiterhin unterstützt haben zu einem Zeitpunkt an dem ich nicht mehr an einen Abschluss meiner Dissertation geglaubt habe.

Ich möchte mich auch bei meinen Kolleginnen und Kollegen unserer Arbeitsgruppe und des ÖISM für die nette gemeinsame Zeit und die gute Stimmung bedanken.

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Meiner Familie und meinen Eltern möchte ich dafür danken, dass sie den Grundstein dafür gelegt haben, dass ich diese Dissertation habe schreiben können und, dass sie immer für mich da sind.

Zu guter Letzt möchte ich mich bei meinen Freunden bedanken, die mich in unseren gemeinsamen Gesprächen unterhalten haben, mir andere Standpunkte dargelegt haben und mich so bereichert und meine Ansichten erweitert haben.

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1. Introduction

1.1. Definitions

For most organisms a well-functioning circulatory system is indispensable. By means of such a system, nutrients and other important substances as well as O_2 can be transported to cells and organs on the one hand, while on the other hand toxic or useless substances like CO_2 can be carted off (Klinke et al. 2005, p. 176).

This chapter is intended to give a better understanding about the basic functions and mechanisms that influence the cardiovascular system and to demonstrate the most important known connections concerning arterial stiffness.

1.1.1. The Cardiovascular System

The circulation of the blood in our bodies is of essential importance in order to facilitate the exchange of different substances and to supply oxygen in organs, tissues and cells.

Within the blood cycle it can be distinguished between a “small” or “lung cycle” and a “big” or “body cycle”, which are connected by the heart. The body cycle transports the oxygen-rich blood, starting at the left ventricle, through the body until it reaches the heart at the right ventricle again. Then the lung cycle transports the meanwhile oxygen-poor blood throughout the lung till it reaches, oxygen-rich again, the left ventricle where the body cycle starts again. These two cycles are also referred to as high-pressure system and low-pressure system. While the left ventricle has to pump the same stroke volume against the high pressure (approximately 120mm Hg) of the body cycle, the right ventricle only has to overcome the pressure of the pulmonary arteries (approximately 20mm Hg) (Klinke et al. 2005, p. 138).

In order to transport the blood through the arterial system, the heart contracts itself in a rhythmically manner according to the physical demands.

The phase in which the heart relaxes and is filled with blood is called diastole whereas the phase in which the heart contracts and ejects the blood is called systole (Klinke et al. 2005, p. 138).

However, the heart is only one part of the cardiovascular system. In fact, the cardiovascular system is composed of three important parts. The heart, the motor, is the first part, which drives the whole system by pumping the blood through the body. The second part ensures the distribution of the blood, which is done by a conduit system. This conduit system consists of arteries, which deliver the blood from the heart to the organs, and tissues and the veins that lead the blood back to the heart. The third part, the capillaries, represents the regions where the oxygen-rich and the oxygen-poor blood are exchanged in all tissues.

The haemodynamic transactions within this system are highly complex, dynamic, non-linear and moreover inconsistent and different in respect of the arterial segment (Weber et al. 2008). Moreover, different arterial segments show different viscoelastic properties, which are non-linear, anisotropic and which show strong abilities to adapt. Furthermore, the blood flow in this system and its pulsatile nature as well as the vessels' complex structure and the permanently changing tone of the smooth muscles in the vessels makes the analysis of the large artery dynamics difficult (Koivistoinen et al. 2007). Therefore, a complete analysis and description of diverse processes regarding the cardiovascular system and its influencing parameters is very difficult and not totally possible.
The main determinant of the pressure in a vessel is the ratio of upstream and downstream resistance (Faraci & Heistad 1990). Alterations in this ratio can change the microvascular pressure. For example, when the arterioles dilate and the large arteries constrict, the pressure in the small vessels decrease without any change in the blood flow. On the contrary, if resistance in the large arteries and in the arterioles increase or decrease in a similar manner, blood flow will change whilst pressure in the small arteries will stay constant (Safar et al. 2012).

Within the cardiovascular system a number of parameters describe and characterize functions and processes. These include heart rate, systolic and diastolic blood pressure, as well as from these derived mean arterial pressure and pulse pressure. The two latter have gained scientific interest during the last years as they have been studied regarding a prognostic value concerning cardiovascular diseases and cardiovascular risk (Chae et al. 1999, Franklin et al. 1999, Safar 2001, Vaccarino et al. 2001, Safar et al. 2002). However, if only one single measurement of blood pressure is to be used, pulse pressure has the least predictive value concerning the cardiovascular risk (Lewington et al. 2002).

Besides these pressure parameters and the heart rate, parameters describing the mechanistic characteristics of arteries, like the stiffness or the distensibility, are considered the most important ones regarding a description of the cardiovascular system's condition. Above all, this is true for the pulse wave velocity of central arteries and the aorta.

1.1.1.1. Blood Pressure

In order to describe certain functions and processes of the cardiovascular system, different pressures within the vessels and this system are used. The most common ones are the systolic blood pressure, the pressure within the vessels during the systole, and the diastolic blood pressure, the pressure within the vessels during the diastole.

Several studies have aimed to find out, which blood pressure parameter or which combination of blood pressure parameters show the best prediction regarding cardiovascular risks, but without a final agreement so far.

The relationship between systolic as well as diastolic blood pressure and cardiovascular diseases, the prediction of these and the risk in connection with these pressure parameters is well established has been used for over a century. Only recently attention to two newer blood pressure parameters has been paid: mean arterial pressure and pulse pressure.

Blood pressure in general, can also be characterized by its pulsatile and its steady components (Darne et al. 1989, Safar 1989). The first one is expressed by pulse pressure whilst the second one is expressed by mean arterial pressure.

The pulsatile component is characterized by blood pressure variations, more exactly as systolic blood pressure and diastolic blood pressure, and, in central arteries, is mostly affected by heart rate, left ventricular ejection fraction and large artery compliance (Franklin et al. 1997, Safar et al. 2011). Mean arterial pressure, the steady component, is the product of cardiac output and vascular resistance and therefore characterized mainly by left ventricular contractility, vascular resistance and elasticity over time and also heart rate (Safar 1989, Benetos et al. 1997a, Safar et al. 2011).

Both, pulse pressure as well as mean arterial pressure, have shown to be independent predictors of cardiovascular events, with mean arterial pressure

being a predictor for overall cardiovascular risk and pulse pressure being a predictor for mainly in coronary arteries artherosclerosis-related complications (Darne et al. 1989, Jankowski et al. 2008).

Besides systolic, diastolic and pulse pressure also mean arterial pressure was significantly associated with total mortality in individuals < 60 years of age. On the other hand, in older individuals only systolic and pulse pressure but not diastolic and mean arterial pressure showed a significantly correlation with total mortality (Hadaegh et al. 2012).

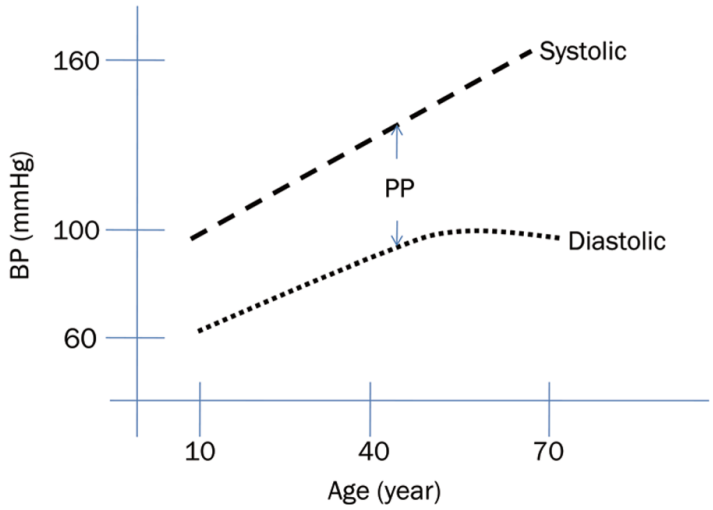

Figure 1: Illustration of the effect of age on systolic, diastolic as well as pulse pressure (PP).
(adapted by the author from Shirwany & Zou 2010)

1.1.1.1.1. Central vs. Peripheral Pressure

Blood pressure measurements at the periphery, for example at the brachial artery level, have been used in the daily clinical practice in order to describe haemodynamic characteristics of the circulatory system for over a century. This is primarily because of its wide availability, satisfactory reproducibility and the established reference values (Schillaci & Grassi 2010). Nevertheless, blood pressure parameters measured at the periphery might not reflect the situation of the central haemodynamic as the periodically oscillating pulse wave generated in the arterial tree undergoes progressive distortion with distance from the heart.

The sites of reflection of the pressure waves are closer to the periphery than to the central arteries, which is why the reflected pressure wave merges with the forward wave closer to the periphery than the central arteries. As a result, the augmentation of the systolic blood pressure is more pronounced in the periphery than in the central arteries like the aorta (Schillaci & Grassi 2010).

The consequence of these phenomena is that the amplitude of the pressure wave is higher in the periphery than in central arteries. Furthermore, amplifications of the pressure parameters between central and peripheral sites are higher in young patients than in older patients. Moreover, these amplifications get higher the more the arterial stiffness increases but also as a result of increased peripheral resistance, the magnitude of the wave reflection and elevated heart rate (Avolio et al. 2009).

The alterations of aortic stiffness caused by physical training also change the relationships between brachial and aortic systolic blood pressure as well as pulse pressure (Laurent et al. 2011). Not least because of this, the question arises whether brachial, peripheral blood pressure gives an incomplete picture of the real, central cardiovascular situation and above all cardiac load and whether central blood pressure could give a better insight (Laurent et al. 2011).

Body height has also shown to influence blood pressure and that shorter stature is correlated with lower amplifications of central as well as peripheral systolic blood pressure (Nakamura et al. 2005).

The pressure that really affects the heart is the central, aortic systolic pressure. It is determined by cardiac factors like stroke volume and ejection time and by arterial factors like stiffness and pulse wave reflection (Janner et al. 2010).

Several epidemiological studies as well as clinical observations have shown a greater importance of central blood pressure parameters, above all pulse pressure, in comparison to peripheral blood pressure parameters. Central parameters, rather than peripheral ones, might be the relevant ones regarding their prediction value of cardiovascular damages or diseases and end-organ-damages (Safar et al. 2002, Chirinos et al. 2005, Williams et al. 2006, Roman et al. 2007, Jankowski et al. 2008, Pini et al. 2008, Wang et al. 2009).

In contrast to mean arterial pressure and diastolic blood pressure, which are almost continual from the central to the peripheral arteries, the systolic blood pressure as well as the pulse pressure increase from the aorta to the peripheral arteries like the brachialis, as a result of increased arterial stiffness and pulse wave velocity. This means that pulse pressure and systolic blood pressure show significant differences in the centre and the periphery (Latham et al. 1985, Nichols & O'Rourke 1998, Weber et al. 2008).
The gap between centrally measured and peripherally measured blood pressure can be as big as 20mm Hg (Wilkinson et al. 2000).
In contrast to the brachial systolic blood pressure, which is not influenced by heart rate, central blood pressure is significantly increased by heart rate reduction, which can be a confounding factor (Lee & Oh 2010).

As pulse pressure undergoes an amplification between central and peripheral arteries, it is inaccurate to use the peripheral parameter as a surrogate for the central parameter (Laurent et al. 2006).
In fact, central parameter values and peripheral parameter values should not be confounded, like for example for systolic blood pressure and pulse pressure. These are overestimated in the periphery regarding to central values, especially in young individuals (Laurent et al. 2005).

Central systolic blood pressure, pulse pressure, augmentation index (AIx) and pulse wave velocity (PWV) are all indexes of arterial stiffness, though, they should not be interchangeably used due to the following reasons (Laurent et al. 2005):

- their determinants are different,
- they can be differently modified like for example by medication or diseased, pathophysiological conditions,
- they are differently sensitive to modifications and changes in other parameters, like for example heart rate or age.

1.1.1.1.2. Pulse Pressure and Mean Arterial Pressure

In general, pulse pressure is a marker of cardiovascular disease and a more reliable parameter and even stronger independent predictor of morbidity and mortality parameter than the more commonly used systolic, diastolic and mean arterial blood pressure parameters in the adult population (Safar et al. 2001, Malone & Reddan 2010). Systolic and diastolic blood pressure have, for a very long time, been considered the only mechanical factors describing the cardiovascular system und predicting the risk of cardiovascular diseases, although they only represent the highest and the lowest points of the blood pressure course (Safar 2008).

Regarding central arterial stiffness, pule pressure is a parameter which only allows the approximate estimation as it also is affected by other parameters like for example stroke volume (Agabiti-Rosei et al. 2007, Shirwany & Zou 2010). Like the systolic pressure and the pressure wave amplitude also the pulse pressure increases towards the periphery, in contrast to diastolic pressure and mean arterial pressure which do not show any significant changes throughout the arterial tree (Laurent et al. 2006). Even more, the pulse pressure is a very important parameter concerning physiological changes due to ageing and pathological, degenerative changes of the large, central arteries (Weber et al. 2008). A widening of the pulse pressure is associated with higher risks of myocardial infarction, stroke and congestive heart failure (Lee et al. 2008).

Although the pressures of the periphery, like brachial artery pressures, are, as a rule, higher than the central aortic pressures, and only crudely represent the latter pressure conditions, central pulse pressure is in part influenced by the elastic properties of the peripheral arteries. This is because the retrograde pressure wave which contributes to the pulse pressure is mainly reflected in the periphery (Williams et al. 2006, Shirwany & Zou 2010).
Central blood pressure and pulse pressure relate more strongly to vascular diseases and predict more all-cause and cardiovascular mortalities than peripheral blood pressure and pulse pressure (Roman et al. 2007, Huang et al. 2011). Furthermore, it’s measurement has become a technically

simple and easy to get surrogate measure of aortic stiffness (Bramwell & Hill 1922).

The degree of the amplification of pulse pressure from central and peripheral arteries is not constant but influenced by several factors like age, posture, exercise and acute heart rate and blood pressure changes (Kroeker & Wood 1955, Rowell et al. 1968, Nichols & O'Rourke 1998, Wilkinson et al. 2000, Wilkinson et al. 2001).

However, peripheral, brachial, pulse pressure is an independent predictor for cardiovascular diseases as well (Benetos et al. 1997b, Franklin et al. 2001, London et al. 2001) and an increase has demonstrated to be an independent predictor of myocardial infarction, congestive heart failure and cardiovascular death (Safar 2008). Nevertheless, brachial pulse pressure is not always a correct reflection of central pulse pressure (Pauca et al. 1992, Wilkinson et al. 2001). This is especially important to know, as central pulse pressure and not peripheral pulse pressure influences important organs like the brain, the kidney or the heart (O'Rourke & Safar 2005). Systemic endothelial function demonstrated a greater correlation with central pulse pressure than with peripheral pulse pressure (O'Rourke & Safar 2005).

Both, systolic as well as diastolic blood pressure increase until approximately 50 - 60 years of age, which is when systolic blood pressure further increases and diastolic starts to plateau or even decline during further aging. With aging, pulse pressure increases due to increased arterials stiffness and PWV (Blacher et al. 1999b, Abhayaratna et al. 2008).

The increased arterial stiffness and the therefore relatively empty central arteries during diastole causes the mentioned decrease in diastolic blood pressure after the sixth decade (Franklin et al. 1997). Simultaneously systolic blood pressure increases due to the increase in arterial stiffness. With the systolic pressure increasing and the diastolic pressure decreasing, pulse pressure increases as well (Malone & Reddan 2010).

This explains why, initially barely showing changes, pulse pressure starts to increase after 50 - 60 years of age (Franklin et al. 1997, Mackenzie et al. 2002). Because of this, pulse pressure might be more important and relevant regarding cardiovascular risk in older people (Franklin et al. 1999).

The aorta remodels throughout childhood as a consequence of somatic growth. In the early childhood, after the first years of life, when the

production of elastic fibres gets started, aortic lumen enlargement requires extracellular matrix remodelling around a fixed content of elastic fibres which increases load and elastin and as a result may transfer load from elastin to the stiffer collagen (Lakatta et al. 2009, Wagenseil & Mecham 2009). As a consequence of a larger diameter, the impedance is reduced which helps keeping pulse pressure in a physiological range. Furthermore, it increases wall tension though increased mean and pulsatile wall tension. This higher tension then may cause increased arterial stiffness. Together, higher pulse pressure is most probably a combination of greater aortic wall stiffness and a higher flow that has exceeded capacity for outward aortic remodelling (Zebekakis et al. 2005, Aggoun et al. 2008, Urbina et al. 2010).

As a large pulse pressure has demonstrated to be a marker of increased arterial stiffness and because of the fact that pulse pressure has shown a close association with left ventricular mass, atherosclerosis as well as carotid intima-media thickness, pulse pressure may constitute a cardiovascular risk factor independently of systolic, diastolic and mean arterial blood pressure (Pannier et al. 1989, Witteman et al. 1994, James et al. 1995, Asmar et al. 1997, Franklin et al. 1997, Matthews et al. 1998).

Nevertheless it has to be kept in mind, that pulse pressure is influenced by other parameters like mentioned before. Furthermore, the physiological amplification that the pulse wave experiences while propagating towards the periphery tends to confound pulse pressure as a good surrogate measure of central stiffness. On the other hand, in elderly this amplifications become less and therefore, in this population, seems to be a more acceptable measure of arterial stiffness in contrast to younger individuals (Shirwany & Zou 2010).
The increased pulse pressure leads again to remodelling of the arterial wall in order to reduce wall stress and the thickening of the intima-media, which closes a vicious cycle (Dao et al. 2005). Furthermore, an increased pulse pressure is an independent predictor for cardiovascular risk itself (Safar 2001).

For mean arterial pressure, being chronically increased results in the increase of thickness of the arterial walls (Shirwany & Zou 2010). This thickening might be the result of compensatory remodelling process in order to withstand the higher mean arterial pressure and it's induced higher wall stress.

1.1.2. The Vascular System

During a lifespan, the arterial system has to withstand powerful loads and mechanical demands. Even during 24h the arterial system runs through large different functional demands. Therefore it is not surprising, that the arteries of an old person show signs of exhaustion and damage (Welsch 2006, p. 236). In fact, the magnitude of the impairment of the large arteries could be seen as cumulative magnitude of all prior expositions towards cardiovascular risk factors (Weber et al. 2008).
The stiffness of arteries and especially the stiffness of the aorta can be seen as measures of the cumulative influence of cardiovascular risk factors with aging on the arterial tree, having limited acute variability and enough inertia to reflect the integrated damage of the arterial wall (Laurent et al. 2006, Nilsson et al. 2009).

The vessels of the cardiovascular system have two main functions. The first one is to ensure the transportation and rhythmic circling of blood through the body and to all tissues and organs, while the second is to enable the exchange of essential respiratory gases (O_2, CO_2).
The vascular system consists of three different vessel types, arteries, veins and capillaries, which have different functions and therefore also show different structure. Moreover, the arteries themselves show different function and structure, depending on the region of the vascular system they are in.

In regard of the temporal-spatial propagation, the blood flow starts at the left ventricle and continuous through the arteries and the arterioles, smaller arteries, passing the capillaries, where the gas exchange in the tissues occurs, starting backwards through the venoles, small veins, and the veins back to the right ventricle.

1.1.2.1. Structure

Three different concentric layers can be recognizes in the general structure of a blood vessel: the Tunica intima (1), the Tunica media (2) and the Tunica externa or adventitia (3) (Tittel 2003, pp. 284 - 299).

1.1.2.1.1. Tunica Intima

As the name says, this layer is the innermost of a blood vessel. On its inner side a very thin and smooth layer, the endothelia can be found. This endothelia layer enables the smooth frictionless flowing of the blood. Underneath the endothelia there are a few elastic fibres which build up the Membrana elastica interna and which builds the border to the Tunica media (Tittel 2003, pp. 295 - 300).

1.1.2.1.2. Tunica Externa

This layer represents the connection of the vessels with the surrounding tissue. The main function of the Tunica externa is the protection against mechanic load like distension. It consists mainly of collagen and elastin fibres, orientated in a specific way, which enables certain changes in length and width of the vessel. The Tunica externa is most pronounced in veins of the extremities (Tittel 2003, pp. 295 - 300).

1.1.2.1.3. Tunica Media

In-between the tunica interna and the Tunica externa lies the Tunica media. This layer consists mainly of circular smooth muscle cells but also of elastin and collagen fibres which condense outwards to the Membrana elastica externa which separates the Tunica media from the Tunica externa (Tittel 2003, p. 296). The Tunica media represents the muscle layer of the arterial walls and, dependent on the region within the vascular system, changes in its structure, being most pronounced in arteries next to the heart and almost not existent in the capillaries. Near the heart, the smooth muscle cells are almost completely replaced by elastic lamellae (Lippert et al. 2006, p. 43) as these arteries have to expand and recoil the most.

1.1.2.1.4. The Endothelia

As previously mentioned, a layer called endothelium covers the inner surface of arteries and blood vessels. This layer works as a structural and functional barrier between the blood cells, and the most inner layer of the arterial wall, the intima. Therefore it prevents adhesion and aggregation of different cells like platelets and leucocytes and as a result is very important to keep a functional normal blood flow (Marti et al. 2012).

Another function of the endothelia is the regulation of the vascular tonus by producing, releasing and balancing different vasodilators and vasoconstrictors like Nitrite Oxide (NO) for example (Furchgott & Zawadzki 1980). The latter is one of the main mediators in the vascular tone and can be released due to stimulation of different stimuli. These can be mechanical like shear stress, physical like heat or cold or substances like bradykinin, acetylcholine and others. A thereby stimulated release of NO by the endothelium results in the intrusion in the arterial wall and the relaxation and dilatation of smooth muscle fibres and myofibrils (Rubanyi et al. 1986).

Furthermore the endothelium has anti-inflammatory and anti-proliferative function.

1.1.2.2. The Veins

The number of veins is larger than the one of arteries. Veins can store up to 85% of the whole circulating blood volume. They have a thin wall and are by far more elastic than the arteries. Their distensibilty can by around 200x the one of arteries. As the pressure predominant in veins is smaller and only about 1/8 of the one found in arteries, they do not need to have thicker vessel walls (Tittel 2003, pp. 284 - 299). Because their function is to lead back the blood to the heart, they are able to contract and therefore increase the cardiac output per minute. On the other side, they are able to relax, store a great volume of blood and therefore reduce the cardiac output per minute. As a result, veins are able to dispense the circulating blood without altering the resistance within the vascular system (Tittel 2003, pp. 284 - 299).

As the veins of the extremities, especially the leg veins, have to cope with higher pressure, due to higher hydrostatic load, these veins have thicker walls. Moreover only the small and medium veins, in contrast to the large, central veins, are able to contract, as the latter do not have a circular muscle layer.

Another specialty of the veins is that, at least in most of them, the layer of the wall that is most distinct is the Tunica externa. This can be explained by the fact, that the veins contain a large volume of blood, but at the same time, the pressure that is exerted onto them by the surrounding muscles is higher than the one within the veins (Tittel 2003, pp. 284 - 299).

1.1.2.3. The Capillaries

The wall of these smallest vessels of the vascular system are extraordinary thin, with diameters between 5 - 25 µm, in order to allow the exchange of respiratory gases in the different tissues, which their main task is. The number of capillaries and the surface they build in order to fulfil their task is around 40 billion and 3500m^2. If all capillaries were open all the time or at once, our circulatory system would collapse, as they can store more blood as is present in our bodies, even in endurance trained who have a larger blood volume. Therefore many capillaries are closed when not needed. As a result of the large surface of the capillaries but the same volume of blood, the flow velocity of the blood through the capillaries is much slower than in the veins or arteries. Taken together, the large surface, the huge number of capillaries and their thin walls as well as the resulting slow flow velocity, these characteristics are necessary for a pronounced exchange of substances between the blood and the different tissues (Tittel 2003, pp. 284 - 299).

1.1.2.4. The Arteries

Whilst the Tunica interna and the Tunica externa are rather weak constructed, the most pronounced layer in the arteries, and especially in the large arteries and the aorta, is the Tunica media. It can be made up of up to 40 layers and is also called Tunica muscularis. In the aorta, the media is build-up of an elastic scaffold and the smooth muscle fibres can only scattered be found. With growing distance from the heart, the arteries, like the Aorta thoracalis and the Aorta abdominalis, show less and less of the elastic scaffold, being replaced by smooth, circular muscle fibres (Tittel 2003, pp. 284 - 299).

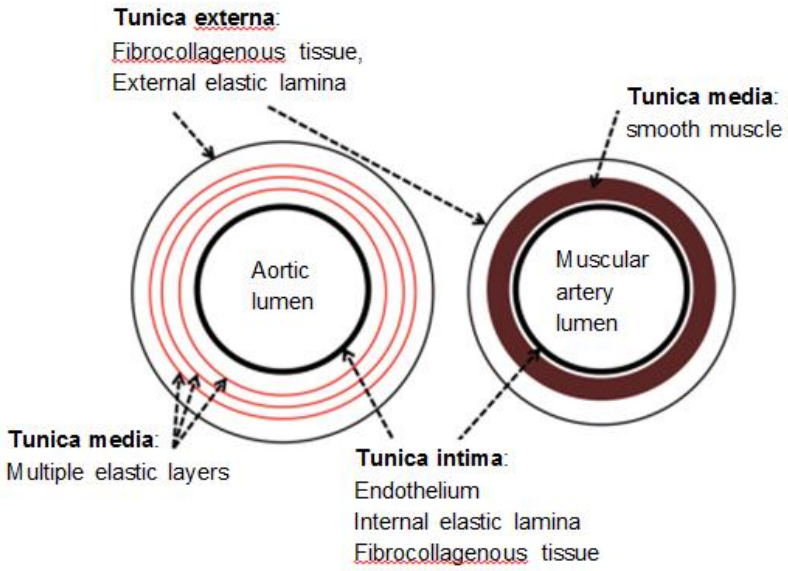

Figure 2: Schematic illustration of an elastic vs. a muscular artery. (adapted by the author from Shirwany & Zou 2010)

1.1.2.5. The Arterial System

The arterial system has two explicit functions. The first is the dampening or cushioning function concerning the blood pressure oscillations caused by the intermittent ventricular blood ejection. The second is the delivery or conductance function concerning the transportation of an adequate blood volume from the heart to the peripheral tissues and organs in accordance to the metabolic demand (Safar 2001, Safar et al. 2003). The degree of this function shows a stepwise increase from the central artery, the aorta, to the periphery (Zieman et al. 2005).

The efficiency of the first function, the dampening function, is besides the geometry, length, width and lumen of the arteries and their endothelium-caused low resistance to flow, mainly dependent on the viscoelastic properties of the arterial walls which can be influenced by endothelium altering factors (Mulvany & Aalkjaer 1990, Kung & Luscher 1995). The importance of the viscoelastic properties is especially true for the central and proximal, large arteries which are the reasons for the “Windkesseleffekt”. When functioning properly, the “Windkesseleffekt” is responsible for the transformation of the pulsatile blood flow, which is a result of the alternating constriction and dilatation of the heart and the thereby caused ejection of blood, in the central

arteries to a steady flow which the peripheral tissues and organs require (Safar et al. 2012). Without this converting “Windkesseleffekt” of the aorta, there would be a pulsatile blood flow with very high and very low pressures in systole and diastole (Lee et al. 2008). The brain, for example, is like the eye and the kidney a high flow organ which is highly sensitive to haemodynamic pulsatility (Mitchell 2008). Some authors state a strong association between arterial stiffness pressure and cerebral perfusion (Kwater et al. 2009, Tarumi et al. 2011, Webb et al. 2012). The recurring exposure of these pulsatile flows and pressures can lead to microvascular hypoperfusion and as a result ischemia and cerebrovascular impairment (Mitchell et al. 2005b).

Several diseases like hypertension, atherosclerosis, hypercholesterolemia, diabetes, cardiac failure or just the process of aging, limit the endothelium-dependent vasodilatation (D'Angelo & Meininger 1994, Matrougui et al. 1998, Levy et al. 2001, Schofield et al. 2002) and therefore decrease the proper function of the arteries, also affecting the “Windkesseleffekt”.

The large, central arteries like the aorta or its large branches are the ones most elastic. The more distal arteries, the peripheral arteries are the ones of highest stiffness. This is mainly due to different components and structure as being described before. In the large arteries, elasticity is, besides others, the result of the components of the extracellular matrix and the elastin-collagen combination, which changes to the contrary on its way to the periphery toward less elastin and more collagen.

The elastic aorta of a young healthy person is able to expand to an extend to store up to 60 - 70% of the blood ejected from the left ventricle. The elastic recoil of the expanded aorta during diastole is then responsible for the continuous, steady blood flow into the small, peripheral resistance vessels (Lee et al. 2008).

The arteriolar branching, then, enables the distribution of oxygen and blood through a steady flow within various organs such as the brain, heart and kidney (Safar et al. 2012).

1.2. Arterial Stiffness

Approximately 90 years ago first steps were taken in the measurement of physiological changes in the properties of arteries in different diseases (Bramwell & Hill 1922). Even longer ago, physicists developed hydraulic and elastic theories of the haemodynamic processes and arterial stiffness. Between 1860 and the beginning of the 20th century physiologists and physicians developed different types of sphygmographs, first devices to asses arterial stiffness so to say, and took first steps in the analysis of pressure waves (Laurent et al. 2006).

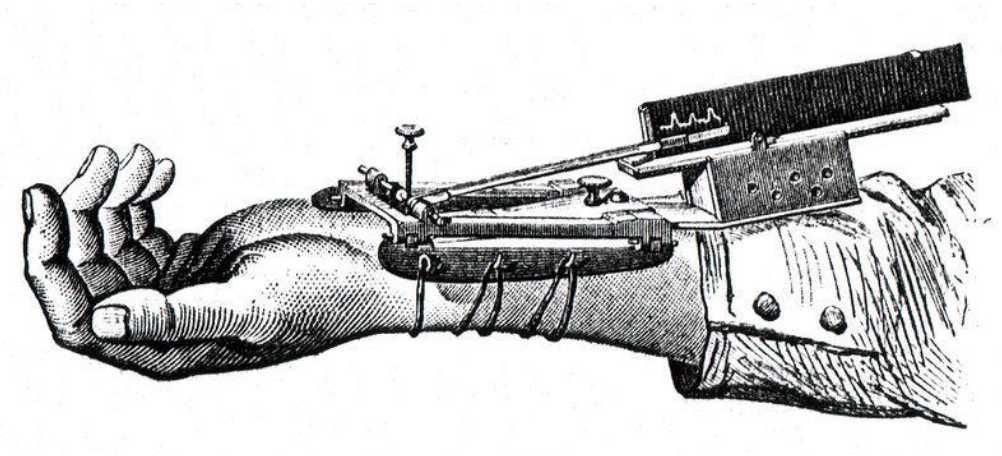

Figure 3: Pictorial representation of one of the first sphygmographs at the end of the 19th century by Étienne-Jules Marey (Marey 1878, p. 281). (http://commons.wikimedia.org/wiki/File:Marey_Sphygmograph.jpg)

Arterial stiffness is a generic term for structural, as well as functional properties of the arterial system (Baulmann et al. 2010).

The stiffness of an artery is, beyond many other ways of defining the biomechanical properties, the most common expression and is defined as the relationship between the change in pressure (ΔP) and the change in volume (ΔV). Therefore stiffness represents the instantaneous slope of the pressure – volume relationship ($\Delta P/\Delta V$) (Quinn et al. 2012).

When the left ventricle ejects the blood volume into the aorta, a pressure pulse is generated which spreads along the arterial tree. The velocity of this pressure wave is determined by the geometric and elastic properties of the arterial wall (Quinn et al. 2012). Furthermore, it has been shown that by an increase in arterial stiffness the PWV increases, too (Farrar et al. 1991). This connection is a result of simple physical properties and laws. An elastic conduit, like a blood vessel for example, in which a fluid is pumped or ejected, is able to expand in order to conceive this fluid volume. In

dependence of the proportions of fluid volume, conduit elasticity and conduit width, different amounts of fluid can be conceived. When the conduit returns to its normal form and extent the fluid volume is steadily transported further along the conduit. If it happens that the conduit in the same system is stiffer and therefore not able to expand to the same extend, the fluid volume is forced further along the conduit with a higher velocity as the time in which the fluid volume is ejected stays the same. Therefore the stiffer a conduit is, the lower is its capacity to conceive and store a certain fluid volume which, as a result, has to be transported faster. The slow velocity in a healthy young artery is due to the fact, that a physical waveform propagates with less efficiency in soft, compliant materials and in this case vessels (Shirwany & Zou 2010).
Normally, in healthy conditions, arteries show a steep increase in arterial stiffness from central arteries to peripheral arteries (Koivistoinen et al. 2007).
Due to the higher content of collagen and elastin fibres but also because of the chronic exposure to augmented arterial pressure, the central arteries in contrast to peripheral arteries, are the ones more susceptible to arterial stiffening (Nichols & O'Rourke 1998).

An increased arterial stiffness and therefore a decreased arterial compliance normally manifests itself in the clinical setting as isolated systolic hypertension and therefore also in an elevated pulse pressure. In younger hypertensive individuals systolic, diastolic as well as mean arterial pressure are correlated with higher risk of cardiovascular morbidity (Shirwany & Zou 2010). In contrast, in older and/or hypertensive individuals cardiovascular and cerebrovascular risk is more closely correlated with pulse pressure and increased PWV (O'Donnell et al. 1997, Chae et al. 1999, Franklin et al. 1999, Kostis et al. 2001, Vaccarino et al. 2001). This suggests that the pathophysiological backgrounds between these two groups of patients are different.

Vlachopoulos et al. (2010a) summarized the clinical utility of PWV measurements, in which the authors of these studies calculated an increased risk for cardiovascular events by 14% with an increase in PWV by 1m/s (Table 1).

Table 1: Risk Ratio (RR; 95% confidence intervals (CI)) for total cardiovascular events per a m/s increase in aortic pulse wave velocity.
(adapted by the author from Vlachopoulos et al. 2010a)

Study	RR (CI)
Blacher et al. (1999)	1.17 (1.06 - 1.30)
Laurent et al. (2001)	1.09 (1.02 - 1.16)
Meaume et al. (2001)	1.19 (1.03 - 1.37)
Pannier et al. (2005)	1.12 (1.03 - 1.22)
Shoji et al. (2001)	1.18 (1.01 - 1.39)
Shokawa et al. (2005)	1.35 (1.13 - 1.61)
Sutton-Tyrrell et al. (2005)	1.03 (1.01 - 1.06)
Wang et al. (men) (2010)	1.21 (1.10 - 1.33)
Wang et al. (women) (2010)	1.30 (1.20 - 1.42)
Willium-Hansen et al. (2006)	1.05 (1.01 - 1.08)
Zoungas et al. (2007)	1.14 (1.07 - 1.22)
Overall	1.14 (1.09 - 1.20)

1.2.1. Arterial Stiffness Assessment, Methods and Parameters

Nowadays there are different parameters and measurement techniques, invasive ones as well as non-invasive ones, to assess the stiffness of arteries. The most common used one is the non-invasive assessment of the PWV (Quinn et al. 2012). Although invasive measurements are the most accurate ways to assess PWV and the arterial stiffness, non-invasive methods are much more appropriate for the clinical practice and epidemiological studies (Weber et al. 2008, Baulmann et al. 2010).

Out of these currently available non-invasive method and parameters for the assessment of arterial stiffness, the PWV and the AIx are the two most common and accepted parameters (Tomiyama & Yamashina 2010). Whilst PWV is an indicator of the stiffness of the artery in which it was measured, most authors agree, that AIx is a parameter indicating the systemic stiffness.

Additionally, central, aortic blood pressures like aortic systolic blood pressure and aortic pulse pressure are used to assess arterial stiffness (Baulmann et al. 2010).

The most common non-invasive way to assess PWV is a tonometric method which was already invented more than 150 years ago (Baulmann et al. 2010). For this purpose a tonometer is used to measure the pulse pressure at superficial arteries like the arteria carotis or the arteria femoralis.

PWV as well as AIx deliver extensive information concerning the arterial tree, its function and structure, and therefore are of great prognostic interest and importance and as a result have high predictive value concerning different cardiovascular diseases (Baulmann et al. 2008).

When the pulse wave, generated by the blood ejection out of the left ventricle, propagates along the arterial tree, a second, late, pulse wave is generated and reflected (Figure 4 and 5). This occurs mostly at points of changing impedance due to constrictions of the arteries and bifurcations, mostly at the transition from the small arteries into the arterioles.

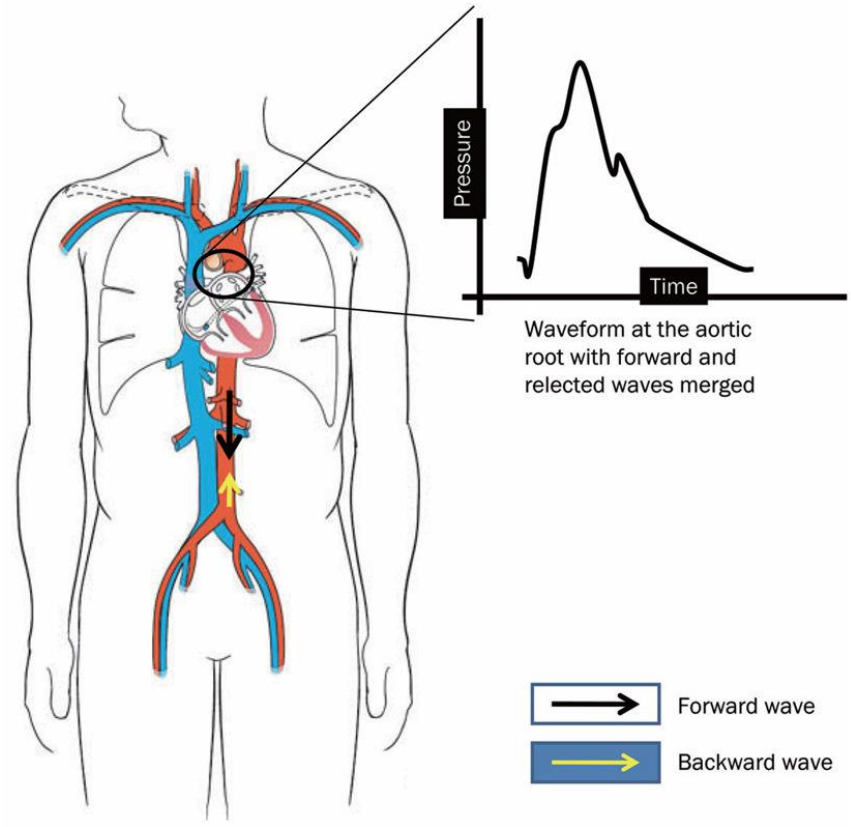

Figure 4: Illustration of the aortic pressure wave form and the concept of the forward and backward propagated wave.
(adapted by the author from Shirwany & Zou 2010)

The magnitude of these reflected pressure waves are dependent of the muscle tonus in the small arteries, the geometry and also the number of arterioles. (Weber et al. 2008, Veijalainen et al. 2011). Whilst the impedance of the elastic arteries is rather static, smaller arteries are more dynamic depending on smooth muscle tone and vessel size (Marti et al. 2012).

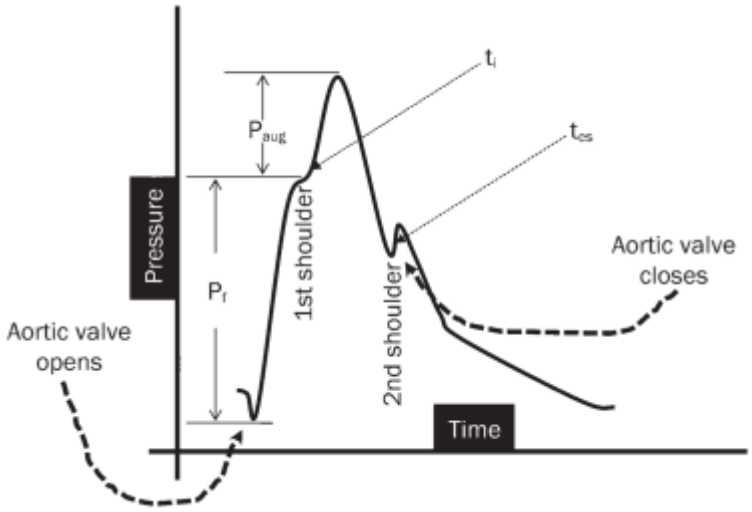

Figure 5: Illustration of the aortic pressure waveform and its key components.
(adapted by the author from Shirwany & Zou 2010)
P_r: Pressure from forward wave; P_{aug}: Augmented pressure from arrival of reflected wave; t_i: Timing of reflected wave; t_{es}: Timing of systolic ejection.

The time point of the reflected pulse wave is dependent of the body height, the heart rate and the PWV. The magnitude of the pulse wave depends of the functional and anatomic condition of the peripheral circulation (Weber et al. 2008). When this second pressure wave travels back the arterial tree towards the heart, it cumulates with the first, the forward, traveling pressure wave. These two merge and build up the augmented pressure wave (Figure 5 and 6). The amplitude of the augmented pressure of the first and the second pressure wave is proportional to the stiffness or the impedance at the reflecting sites. Moreover, the time point of the pressure peak is related to the PWV and the distance to these sites.

A disparity between central and peripheral, muscular arteries can be seen regarding the width and elasticity, which are decreasing from central to peripheral arteries, causing the increase in arterial stiffness from the centre to the periphery.

This means that, pulse pressure for example, measured at the periphery might not reflect the pressure situations found in the aorta (Lee et al. 2008).

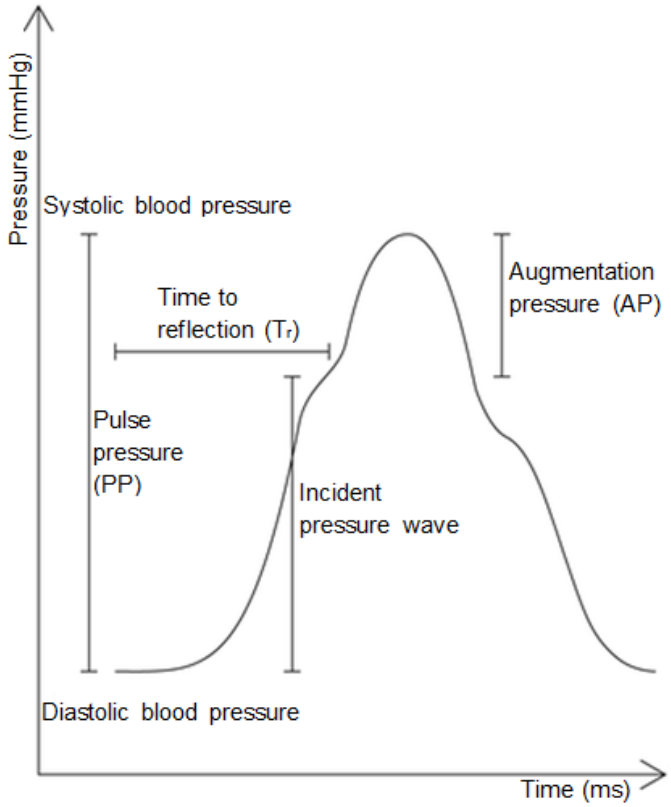

Figure 6: Illustration of the pulse wave analyses and the derived measures.
(adapted by the author from Janner et al. 2010)

As the walls of the aorta contain a high proportion of elastin, they allow a huge distension during systole, in contrast to the distal, muscular arteries, which show a high proportion of collagen fibres and are therefore less distensible. These different characteristics explain why the arterial tree experiences a progressive increase in stiffness and as a result a decrease in pulsatility from central arteries to the periphery. This minimizes the risk of barotrauma that would result if the smallest arteries and the microcirculation of organs like the brain or the kidney would be exposed to peak systolic pressures. Alterations in the arterial pulsatility leads to increased shear stress which affects endothelial function, a lower production of Nitric Oxide and therefore could cause the development of atheromatous plaques through vessel wall remodelling (Glagov et al. 1988). Moreover, stiffer arteries with less pulsatility have higher risk for stroke or renal impairment due to higher pressure fluctuation in their vasculature (Quinn et al. 2012). Increased pulsation as a result of stiffer large arteries is led until the microcirculation where they cause severe damage (Weber et al. 2008).

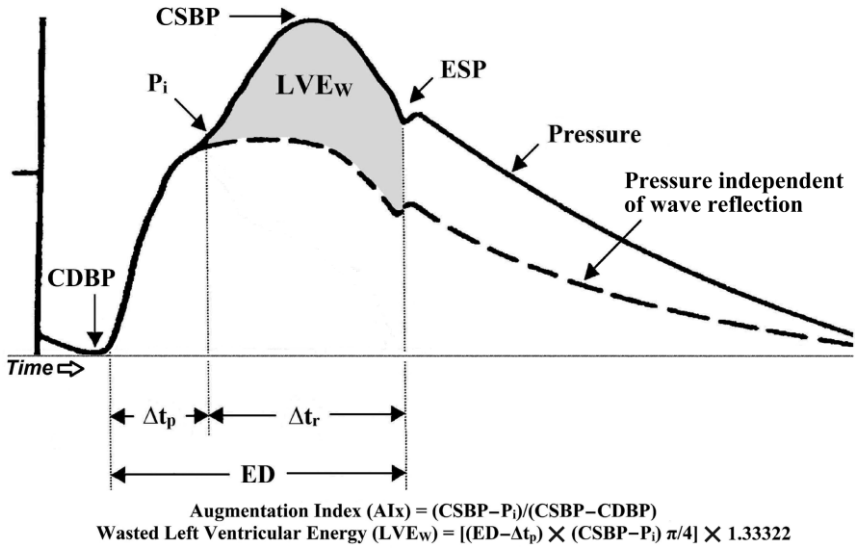

Figure 7: Illustration of a typical central aortic pressure wave form synthesized from the radial artery pressure wave form using applanation tonometry, with superimposed wave form of aortic blood flow.
In this illustration the broken line represents the theoretical aortic pressure wave form which would occur without any wave reflection. The solid line represents the real aortic pressure wave form (adapted by the author from Beck et al. 2013).
Central aortic systolic blood pressure (CSBP), Central aortic diastolic blood pressure (CDBP), Wasted left ventricular pressure energy (LVEw), Ejection duration (ED), End systolic pressure (ESP), Δt_p round trip travel time of the reflected pressure wave to the major peripheral reflecting site and back to the aorta, Δt_r systolic duration of the reflected aortic pressure wave, P_i onset of the reflected aortic pressure wave.

In fact, an increase in stiffness of the central arteries, referred to as arteriosclerosis, is associated with different negative cardiovascular changes in healthy people but also in people with different diseases (Laurent et al. 2006, Vlachopoulos et al. 2010a). The stiffening of the aorta is a normal development during the process of aging and the main reason for isolated systolic hypertension in older individuals (Izzo 2004). Moreover, besides older individuals, also in adolescents and young adults, isolated systolic hypertension (ISH) is the predominant form of hypertension. Though, there is a difference in the underlying pathophysiology, being an increased stroke volume in young men and increased aortic impedance, due to a smaller aortic diameter, in young women, whereas in individuals older than 50 - 60 years of age this is caused by increased arterial stiffness (Lee et al. 2008).

In all populations, even in those where arteriosclerosis seldom arises, the stiffening of the arteries is a progressive development with age (Avolio et al. 1985). The stiffening of the aorta leads to different pathophysiological changes within the circulation and is linked to several cardiovascular diseases. Most of all, a stiffer aorta is no longer able to accommodate the blood volume ejected by the left ventricle.

The normal, physiological cushioning function decreases with distance from the heart, being highest in the ascending aorta and lowest in the peripheral arteries. Likewise the PWV is different in the different arterial segments, due to the decreasing elasticity from the central to the peripheral arteries but also due to differences in the molecular, cellular and histological structure (Weber et al. 2008).

Normally, in a young and healthy arterial system, the reflected pressure wave reaches the aortic root, the ascending aorta and the heart during diastole of the same heart cycle and therefore augments the coronary circulation and perfusion, whilst in a diseased arterial system this happens in the late systole of the same heart cycle (Nichols et al. 1985, Weber et al. 2008, Sako et al. 2009).

In the first, the healthy case, the diastolic pressure is increased and therefore the perfusion of the heart is maintained. In the second case, the diseased, when the PWV of the aorta is increased the pressure wave arrives earlier, in the late systole of the same cycle, when the ventricle is still ejecting blood into the aorta, the heart has to work against a higher pressure which increases the afterload and therefore leading to an augmented central systolic blood pressure as well to an increased aortic pulse pressure, resulting in a left ventricular hypertrophy and a higher oxygen demand (Weber et al. 2008). The fact that the PWV increases with the reflected pulse pressure reaching the ascending aorta already in the systole when getting older explains why systolic blood pressure and pulse pressure increases while diastolic blood pressure decreases. This suggests that systolic blood pressure in the aorta determines the cardiac afterload and that the diastolic blood pressure is a relevant parameter for the corona perfusion.

Furthermore, the earlier return of the pulse pressure results in a decreased central diastolic blood pressure which causes a reduced cardiac perfusion and therefore can result in a myocardial ischemia (Weber et al. 2008).

The increased pressure leads to increased arterial wall stress, progression of arteriosclerosis and the hypertrophy of the left ventricle due to an increased left afterload (Nichols et al. 1985, Sako et al. 2009). All together can increase the risk for cardiovascular diseases (Safar 2001, Lee et al. 2008).

1.2.1.1. Pule Wave Velocity (PWV)

PWV is the velocity of the pulse wave which spreads out from the heart towards the peripheral arteries. PWV shows an inverse correlation with the distensibility of the arteries. In order to measure PWV, the time needed between two determined segments, usually between the arteria carotis communis and the arteria femoralis, is measured and as the distance between these two points can be measured as well, the PWV can be calculated. If the time interval between the pulse wave at two different arterial sites is measured, and the distance between this two sites is known, PWV can be calculated as:

Velocity (m/s) = distance (m) / time (s).

The measurement of the PWV between the arteria carotis communis and the arteria femoralis is considered the gold standard as it is a simple, direct, robust, non-invasive and well reproducible method (Baulmann et al. 2008, Weber et al. 2008). Additionally, the arterial stiffness measurement of the aorta, like the Carotid-femoral PWV, has been recommended in 2000 at the first consensus conference on arterial stiffness, and has shown the most significant prediction value in pathophysiological outcome data (Laurent et al. 2006, Mancia et al. 2007, Vlachopoulos et al. 2010a).
However, PWV can be measured between any two regions of the arterial tree and therefore can reflect the elasticity of this segment (Figure 8).
The PWV in humans increases approximately from 4 - 5m/s in the ascending aorta to 5 - 6m/s in the abdominal aorta and up to 8 - 9m/s in the iliac and femoral arteries (Latham et al. 1985).

Nevertheless, the clinical value and use of PWV measurements is hampered and restricted due to limited availability of normative and reference group data and further, by different techniques and methods for the PWV measurement (Laurent et al. 2001, Meaume et al. 2001, Boutouyrie et al. 2002, Pannier et al. 2002, Safar et al. 2002, McEniery et al. 2005, Khoshdel et al. 2006, Laurent et al. 2006, van Popele et al. 2006, Mancia et al. 2007, Rajzer et al. 2008, McEniery et al. 2010a, McEniery et al. 2010b).
Carotid-femoral PWV, as the most widely used method to assess aortic PWV, is an independent predictor of cardiovascular mortality and morbidity in different populations (Meaume et al. 2001, Mattace-Raso et al. 2006, Willum-

Hansen et al. 2006, Inoue et al. 2009, Mitchell et al. 2010). Physiologically, the wave form at the proximal aorta determines the left ventricular load and the coronary blood flow more and better than the peripheral blood pressure (Westerhof & O'Rourke 1995).

Nevertheless, brachial ankle PWV has also shown to be an independent predictor of cardiovascular death and events in different populations and it is a little easier to assess (Matsuoka et al. 2005, Tomiyama et al. 2005). Though, there is one important limitation to brachial ankle PWV interpretation, as it is significantly influenced by blood pressure. Blood pressure increases arterial wall tension and therefore adds functional stiffening to the arteries which makes blood pressure a confounding variable concerning the arterial wall stiffness (Lee & Oh 2010).

The PWV is inversely correlated with the arterial compliance. Consequently, PWV is a matter of the arterial stiffness of a certain arterial segment. As the aorta, the most central and most elastic artery, is responsible for most of the cushioning function, changes of the stiffness in this region affects the heart the most. Not at least this makes the assessment of the aortic, central arterial stiffness the most important one with regard to cardiovascular diseases (Weber et al. 2008).

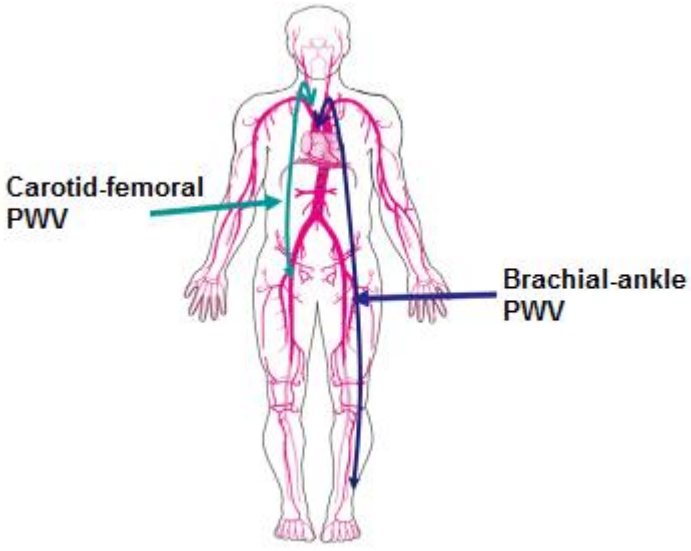

Figure 8: Illustration of two measurement techniques at the carotid-femoral PWV and the brachial-ankle PWV. (adapted by the author from Tomiyama & Yamashina 2010)

In contrast to adults, in which several studies have already focused on the influences of sports exercise on arterial stiffness, acute as well as chronic, and on establishing reference values for PWV, in children and adolescents such data and studies are scarce. In fact, data on the acute effects directly after a sports exercise to exhaustion on the arterial stiffness in children and adolescents are missing.
However, in children and adolescents some authors suggested PWVao values at rest between 2.6 – 6.2m/s (Schack-Nielsen et al. 2005, Sakuragi et al. 2009, Reusz et al. 2010).

1.2.1.2. Augmentation Index (AIx)

The augmentation index of the aorta was first derived by Murgo et al. (1980) and defined as the ratio of augmentation pressure to pulse pressure. Then, AIx could only be measured invasively and it was Kelly (1989) who developed a non-invasive, but peripheral, measurement by applanation tonometry. In 1996 O'Rourke & Gallagher develop the measurement further in order to measure the central AIx non-invasively.
Noninvasively measured central blood pressure indices like AIx have been proven to be able to predict the onset of cardiovascular diseases and all-cause mortality by several studies (Williams et al. 2006, Vlachopoulos et al. 2010a).

Augmentation pressure constitutes the difference between the first, orthograde, towards the periphery flowing systolic peak and the second, retrograde due to reflections and bifurcations, mainly in the range of the capillaries, towards the heart flowing systolic peak. Both, the first and the second pressure peak, are being added and summed up and the earlier the second pressure peak returns the higher is the fused pressure wave and the AIx. The AIx is expressed as percentage of the augmentation pressure from the pulse pressure amplitude (systolic BP – diastolic BP = 100%) (Magometschnigg 2008).
In fact, the quantification of the contribution of the reflected wave on the arterial pressure wave is the AIx (Segers et al. 2005). It reflects the ratio of the forward pressure wave and the reflected pressure wave and can be used in order to estimate the central blood pressure (O'Rourke & Hashimoto 2007, Tomiyama & Yamashina 2010, Vlachopoulos et al. 2010a).

Nevertheless the validity of this parameter as an index of the arterial stiffness is still controversy as studies have shown that AIx is not always a reliable surrogate parameter of arterial stiffness (Kelly et al. 2001, Lacy et al. 2004, Williams 2004).

Although showing inhomogeneous results in some studies, the AIx showed to be closely related to the physiological arterial aging as well as to abnormal aging of the arteries due to different diseases (Lacy et al. 2004).

AIx is, besides arterial stiffness, also dependent of other factors, like for example peripheral vasoconstriction or PWV and the amplitude of the reflected pulse wave (Kelly et al. 2001, Mitchell et al. 2005a).

AIx is also influenced by blood pressure and heart rate (Wilkinson et al. 2001, Williams et al. 2009, Lee & Oh 2010). For this reason, AIx sometimes is corrected for heart rate (Wilkinson et al. 2000), although this is not undisputed, as a Pubmed database search revealed several studies with several different results regarding differences in the use of AIx or AIx corrected for heart rate (Stoner et al. 2014).

Weber et al. (2008), furthermore, states age, body height, gender, heart function, cardiovascular risk factors and medication as additional parameters relevant for influencing AIx.

The observed increase in AIx before the age of 60 years is the result of an earlier wave reflection. Whereas the first pressure wave is almost unchanged, the augmentation pressure increases systolic pressure resulting in the increased AIx. However, after the age of 60 years, the first pressure wave starts to contribute to the increasing systolic pressure to a similar extend as does the augmentation pressure. As now the augmentation pressure accounts to a smaller percentage of the pulse pressure, the AIx levels off (Janner et al. 2010). The plateau in AIx seen in ages above 60 years is at least in part the result of impedance mismatching between the elastic, central and muscular, peripheral arteries (Vyas et al. 2007, O'Rourke 2009). Another reason could be that arteries then stop further stiffening. However, as PWV increases with age, this indicates that arteries are still getting stiffer after that age and that the reason for the AIx plateau is found maybe in the construction of this parameter (Janner et al. 2010).

However, the quantity of the influence of each of these factors can vary and in healthy individuals, for example, with compliant arteries, AIx is influenced to a

higher extend by the magnitude of the reflected wave than by the velocity of the reflected wave in contrast to individuals with increased arterial stiffness (Kelly et al. 2001).
AIx reflects the stiffness of the systemic arterial tree (O'Rourke 1990, Nichols 2005, Segers 2008, Stoner et al. 2014) and in contrast to the PWV constitutes an indirect marker of the stiffness of arteries, but a direct marker for the wave reflection (Laurent et al. 2006, Baulmann et al. 2008).
Cheng et al. (2007) postulated, that AIx is no sensitive surrogate for changes in the central pressure wave form, which indicates a change in large, central arterial function.
Other authors state that, AIx serves as an effective marker and is an indicator of central, aortic stiffness (Kelly et al. 2001, Garcia-Ortiz et al. 2010).

Several studies have demonstrated a higher AIx in women than in men (London et al. 1995, Yasmin & Brown 1999). Although this is probably due to the fact, that AIx inversely correlated with body height (Smulyan et al. 1998, Wilkinson et al. 2000, Wilkinson et al. 2001, Wilkinson et al. 2002, Janner et al. 2010), other studies have demonstrated that this result can only be partly explained by the lower body height as even after adjustment for body height women demonstrated higher values (Yasmin & Brown 1999, Gatzka et al. 2001, Mitchell et al. 2004).

Again, in adults several studies which investigated AIx regarding reference values and the influences of sports exercise on this parameter exist in contrast to children and adolescents for which such data is scarce. To our knowledge only one very recent study exists investigating AIx in children and adolescents ages 10 – 19 years (Lowenthal et al. 2014). In this study, average AIx values of 3.06 ± 9.51% were postulated. However, studies regarding acute effects directly after a sports exercise to exhaustion on the AIx are still missing.

1.2.1.3. Devices

These days several devices for the assessment of arterial stiffness are commercially available (Table 2), which differ largely according to their physical base, simplicity of use and characteristics of the measured parameters as well as their size and transportability (Boutouyrie et al. 2014). Beyond these different devices, the Complior and Sphygmocor systems are the ones longest available and have been used in several studies, clinical trials and population surveys.

Nevertheless, a number of alternative devices have been developed in the last years.

Table 2: Overview of the most common methods and devices to estimate arterial stiffness.
(adapted by the author from Boutouyrie et al. 2014)

Techniques	Manufacturer	Probe
Direct PWV measurement		
Complior	Alam Medical, Fr	Standard
Sphygmocor	AtCor Medical, Au	High fidelity
PulsePen	Diatechne, It	High fidelity
PulseTrace	Micromedical, UK	Doppler
Vicoder	Skidmore Medical, UK	Cuff
Vascular Explorer	Enverdis, De	Cuff
Ankle-Brachial PWV		
Omron VP-1000	Omron Medical, Jp	Cuff
Q-KD	Novacor, Fr	Cuff
Echo-tracking techniques		
Artlab System	Esaote, It	
E-Tracking	Aloka, Jp	
HDI-lab	Philips, Nl	
Indirect techniques		
VaSera VS-1500N	Fukuda Denshi, Jp	Cuff
CVProfilor	HDI, US	Cuff
Arteriograph	Tensiomed, Hu	Cuff
Mobilograph	IEM healthcare, De	Cuff

The device used in this study is the Arteriograph system.

One of the main advantages of the Arteriograph is, that by using only one simple arm cuff PWVao, AIx, aortic systolic blood pressure and peripheral blood pressure can be measured simultaneously within only 2 - 3 minutes (Horvath et al. 2010).

1.2.2. Influences on Arterial Stiffness

Several studies have proven that arterial stiffness is influenced by many factors. This stiffening of the arteries can occur due to changes in the very complex interplay of independent and inter-dependent factors as well as a consequence of intrinsic factors like different blood pressures, shear stress or other haemodynamic forces as well as extrinsic factors like cardio-metabolic abnormalities (Wildman et al. 2003, Schram et al. 2004), nutrition and especially sodium intake (Safar et al. 2009), hormonal milieu, glucose regulation and the glycaemic state but also as part of a naturally decline in cellular function and systems as comes along with the process of aging (Bassiouny et al. 1994, Beattie et al. 1998, Galis & Khatri 2002, Mitchell et al. 2004, Zieman et al. 2005).

Besides that, several other factors, lifestyle factors, like smoking and alcohol habits have been recognized to alter arteries and to increase their stiffness in an extrinsic way. Moreover, overweight, diabetes, dyslipidaemia as well as physical activity and the cardiorespiratory fitness state have shown to influence the arterial stiffness (Boreham et al. 2004).

Both, pulse wave velocity, as well as AIx show alterations during the process of aging. In young, healthy people, changes in arterial stiffness may be a result of normal structural wall changes and wall stiffening during aging (Glukhova et al. 1991).

Arteries show a natural increase in arterial stiffness in the cause of aging due to, for example, different modifications in the structure of the arterial wall like a decrease in elastin fibres, an increase in collagen fibres or the deposit of calcium.

Even in children and young adults, arterial stiffness assessments are of importance as cardiovascular diseases and events can already occur in this group

of age and it has been shown, that aortic enlargement and impaired aortic elasticity and function can cause several cardiac and non-cardiac diseases (Grotenhuis et al. 2008, Grotenhuis et al. 2009, Kuhn et al. 2009, Voges et al. 2010).

Before evidence was found, that functional and structural changes in the arteries are accelerated when found together with cardiovascular diseases, it was thought, that these changes are normal in the cause of aging (Lee & Oh 2010).

Aging brings along numerous changes in the whole organism and therefore also in the cardiovascular system and in arterial stiffness. These alterations can be of functional as well as structural nature and there is hardly any system, parameter, function or structure that does not show significant changes during a lifetime.
As aging summarizes and includes a great number of these changes and could per se be seen as a contributor and cause for the stiffening of arteries, in this work the processes and changes that are stuck behind growing older shall also be explained for themselves.
Therefore, some of the major mechanisms and parameters influencing arterial stiffness, found in the literature, shall be described in the following chapter. Nevertheless, aging and aging-related changes per se will be described.

1.2.2.1. Aging

There are several functional, morphological and structural changes that lead to a stiffening of the aorta in the cause of ageing, like for example, fragmentation and loss of elastin, calcification, increase in inflammatory cytokines, activation of the renin-angiotensin-aldosterone system, increased salt sensitivity, endothelial dysfunction or increased production of integrins and metalloproteinases (Najjar et al. 2005).
In the process of aging, the vessels dilate and the arterial walls stiffen, mainly due to luminal enlargement with wall thickening and a reduction of the elastic properties (Virmani et al. 1991, Lakatta 1993, Nagai et al. 1999, Izzo & Shykoff 2001).
The reasons for this stiffening are largely found in the media which shows the most degeneration. The arterial pulsation seen over the years cause the elastin fibres to fatigue and to break (Lee & Oh 2010).

As the enormous elastic abilities of the aorta depend mainly of the elastic fibres in its wall this could account for the aging related loss in distensibility, as the maximum rate of elastic fibres occurs in the perinatal period and thereafter starts to decrease, even during childhood (Martyn & Greenwald 1997).
Moreover, these changes are not consistent over the whole arterial tree, being more prominent in the central, large arteries and less prominent in the muscular, peripheral arteries which show no stiffening (Mitchell et al. 2004).

Another reason for the stiffening is the deposition of calcium, especially after the 5th decade (Atkinson 2008). In the process of aging elastin gets fragile, cracks and is compensated by collagen (Kass 2002, O'Rourke & Nichols 2005, Santhanam et al. 2008). Figures 9 and 10 show different wave forms dependent of the age. Besides structural and developmental changes during aging, changes in wall mechanics and stress might be important factors, too (Voges et al. 2012).

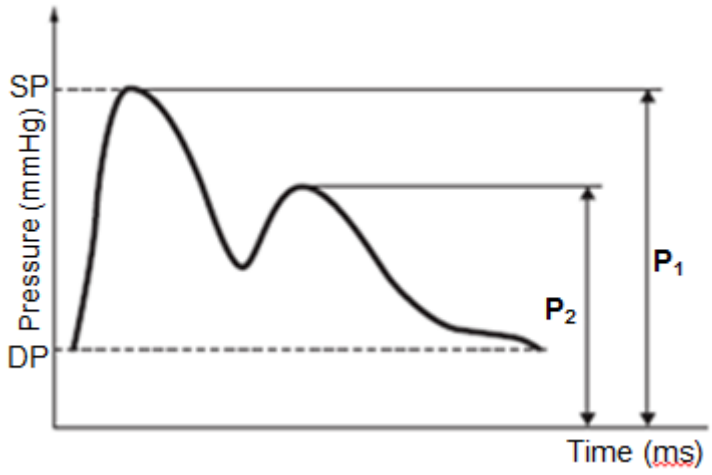

Figure 9: Illustration of a typical wave form of central aortic pressure in younger people (<40 years of age). (adapted by the author from Cheng et al. 2007)
P1 central initial peak, generated by cardiac ejection; P2 central second peak, generated by the reflected wave; SP central systolic blood pressure; DP central diastolic blood pressure.

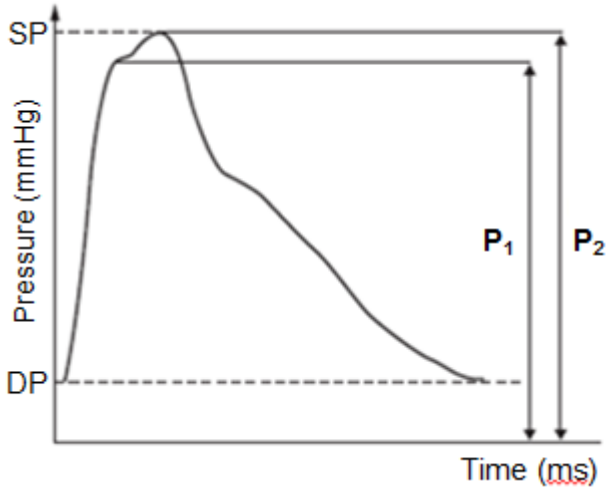

Figure 10: Illustration of a typical wave form of central aortic pressure in older people (>40 years of age). (adapted by the author from Cheng et al. 2007)
P1 central initial peak, generated by cardiac ejection; P2 central second peak, generated by the reflected wave; SP central systolic blood pressure; DP central diastolic blood pressure.

Although most studies state, that PWV and AIx show an linear, age-related increase, this does not necessarily must be the case in central AIx and PWVao which seem to be differently affected by aging (McEniery et al. 2005). Whereas AIx shows more prominent changes in a younger population (<50y) and even actually declines after the age of 60 years, PWVao showed changes in people >50years (Mitchell et al. 2004, Lee & Oh 2010).

Moreover, some studies suggest, that the increase in aortic stiffness with aging is more particular in women than in men (Fantin et al. 2007, Vermeersch et al. 2008). In fact, AIx is higher in women mainly due to their smaller body height which means a closer physical proximity between the heart and the reflecting sites (Mitchell et al. 2004, Fantin et al. 2007). Another study found out, that there is a difference between the rapidness in which PWV increases in central and in peripheral arteries in the process of aging, being higher in the central arteries, in women, in contrast to men, where no difference was found (Vermeersch et al. 2008).

1.2.2.2. Collagen Elastin and Muscle Fibres

As described before, two main proteins, elastin and collagen, build up the vessel walls and are therefore influencing the stiffness of arteries. A fine-tuned balance between these two proteins, depending on where in the system the artery is found, maintains different elastic properties from central, elastic, aortic arteries to stiff, peripheral arteries. Certain imbalances and anomalies due to diseases or aging for example lead to alterations in these elastic properties. Further, increased luminal pressure or inflammatory processes, for example, lead to a decrease in elastin and increased production of collagen (Xu et al. 2000, Johnson et al. 2001). As a result, all these changes lead to increased arterial stiffness.

Additionally, increased arterial stiffness is caused by stiffening of the smooth muscle cells themselves by increased adhesion molecule expression. In the smaller, more peripheral, arteries the stiffness is influenced by hypertrophy and smooth muscle tone (Intengan & Schiffrin 2000, Qiu et al. 2010).

Immunohistochemical and ultrastructural studies have shown that, besides the quantity and quality of stiff wall material, arterial stiffness is also influenced by its spatial organization (Laurent et al. 2005).

1.2.2.3. Endothelial Dysfunction

Both, endothelial dysfunction as well as arterial stiffness have been identified as risk factors for cardiovascular diseases (Blacher et al. 1999a, Schachinger et al. 2000, Boutouyrie et al. 2002, Bonetti et al. 2003).
The endothelia of the vessels play a very important role in the regulation of their stiffness as it produces and controls different vasoconstrictors as well as vasodilators. Dysfunctions of the endothelia or impairments of its regulation tasks between certain vasoactive substances, like an imbalance between Nitrite Oxide (NO), one of the most important vasodilators, and Endothelin-1 (ET-1), one of the most important vasoconstrictors, can manifest themselves for example in changed vasodilatory responses to acetylcholine and therefore increasing the arterials stiffness (Taddei et al. 1995).

Several studies have not only proven relationships with these and other vasoactive substances and aging and/or cardiovascular diseases but also with physical activity. Maeda et al. (2003) for example found out, that ET-1 increases when getting older and Otsuki et al. (2007b) showed an increase in the ET-1 concentration in conjunction with certain cardiovascular diseases.

Different types of physical activity have also proved to have different consequences on the production and function of vasoactive substances. Whilst endurance training has shown to reduce the concentration of ET-1 and therefore an important vasoconstrictor (Maeda et al. 2001, Maeda et al. 2003), ET-1 has shown to be increased in resistance trained individuals (Otsuki et al. 2006). Moreover these resistance trained individuals also showed increased arterial stiffness which suggests that the increased arterial stiffness is, at least in part, due to the increase in ET-1 concentration. Also, NO concentration showed to be increased in endurance trained individuals with an increased NO bioavailability (Kingwell et al. 1997b, Higashi et al. 1999, Goto et al. 2003, Maeda et al. 2001, Maeda et al. 2004).

On the contrary, the reduction in ET-1 concentrations due to endurance exercise is thought to contribute to, and be responsible for, the favourable changes on the cardiovascular system which are found in connection with physical activity (Maeda et al. 2003).

Further, norepinephrine concentrations could be increased as a result of strength training and as a consequence lead to chronically elevated sympathetic adrenergic vasoconstrictor tone and associated arterial stiffness (Pratley et al. 1994, Raastad et al. 2001).

Therefore, endothelia-derived substances like the vasoactive NO and ET-1 have great influence on the stiffness of the arteries and seem to be, at least in part, responsible for certain, exercise-dependent alterations in the stiffness of these vessels. This suggests, that physical exercise might have a positive, regulatory influence on an impaired, diseased function of the endothelia and therefore could decrease arterial stiffness.

Moreover, it is also possible that an already increased arterial stiffness can contribute to an endothelial dysfunction which then leads to before mentioned impairments and therefore representing a vicious circle.

1.2.2.4. Glucose, Insulin and Neuroendocrine Signalling

The stiffness of arteries is also correlated with insulin resistance and studies have shown, that chronic hyperglycemia and hyperinsulimenia influence renin-angiotensin-aldosterone-axis as well as the angiotensin type 2 receptor expression in the vascular tissue and as a result leading to hypertrophy and fibrosis which means higher arterial stiffness. Alterations of the vasoelastic properties of the arteries are also known as a consequence of an impaired glucose tolerance which increases the glycation of collagen (Nickenig et al. 1998, Jesmin et al. 2003).

Furthermore, angiotensin II is known, for example, to have influence on the production of collagen or the hypertrophy of vessels which, as a result, affects the stiffness of arteries (Dzau 1986).

The vasotone also influences the stiffness of the arteries, although showing more influence on the central, elastic arteries and less influence on the peripheral, muscular arteries (Weber et al. 2008).

Although the arterial wall of the peripheral arteries only shows minor effects in the process of aging, the intima-media can show thickening, as a result of changed vasomotor function, and can therefore contribute to higher peripheral resistance (Hayoz et al. 1992, Taddei et al. 2001). Endurance training for example improves heart rate variability, an indicator of autonomic nervous system function and resistance training has shown to elevate catecholamine levels and to activate the sympathetic nervous system (Pratley et al. 1994). Therefore it is argued that an imbalance between of the autonomic nervous system, as a result of an increased sympathetic and a decreased parasympathetic level can elevate arterial stiffness. (Yoon et al. 2010).

The age-associated stiffening of the arteries as a result of changed vascular structure and function is due to a change in autonomic as well as local vasoactive substance activity (Seals et al. 2006).

The stiffness of medium sized peripheral arteries is also modulated by the vasomotor tone, which is dependent of the endothelial function and/or the sympathetic nervous system and/or the renin-angiotensin system (Boutouyrie et al. 1994, Giannattasio et al. 1995, Giannattasio et al. 2005).

1.2.2.5. Blood Pressure and Heart Rate

Evidence exist that the arterial stiffness of the large arteries increases with increasing blood pressure, too. This is one of the reasons why arterial hypertension often goes hand in hand with higher arterial stiffness, as a higher pressure forces the arterial wall to adapt and therefore recruit more inelastic collagen fibres (O'Rourke et al. 2002).

For AIx, a dependency of heart rate has been demonstrated. In a study by Wilkinson et al. (2000) a significant and linear reduction in AIx following an incremental pacing in heart rate from 60 - 110 was observed. Only above a heart rate of 120 this correlation became non-linear. Similar results showed a study by Stefanadis et al. (1998). Wilkinson et al. (2002) stated that the heart rate-depending reduction in AIx is a mathematical manifestation of a shorter ejection duration and as a result an altered pulse contour, rather than a decrease in arterial stiffness per se. As an increase in heart rate will cause a shorter duration of systole, the time point of the wave reflection reaching the heart again shifts into diastole and therefore reduce AIx (Wilkinson et al. 2000,Wilkinson et al. 2002).
Another study (Sa Cunha et al. 1997) confirms the statement that AIx is influenced by heart rate as a high resting heart rate was correlated with increased arterial stiffness.
Nevertheless, studies indicate an independence of large artery stiffness from changes in heart rate within a physiological range (Bergel 1961, Noble et al. 1967, Nichols et al. 1977) which suggests that changes in the aortic stiffness are not responsible for the relationship between AIx and heart rate (Wilkinson et al. 2000).

1.2.2.6. Gender

Evidence exist that arterial stiffness might also be dependent of the gender. In a study in which women have been analysed, potentially positive effects of resistance training on arterial stiffness could be found (Okamoto et al. 2009).
A study by Collier et al. (2011) showed increases in central arterial stiffness as a result of resistance exercise only in men but not in women. Furthermore they

could show a decrease in central arterial stiffness but no change in peripheral arteries in both, men and women.
Endurance training on the other hand seems to provoke similar effects, decreases in arterial stiffness and other favourable effects on the vascular system in both, men and women (Tanaka et al. 2000, Thompson et al. 2003, Hayashi et al. 2005, Seals et al. 2008).

In general, even in the absence of diverse cardiovascular diseases, women seem to show greater age-related increases in arterials stiffness than men (Redfield et al. 2005) and authors like Koivistoinen et al. (2007), Albaladejo et al. (2003) or Mitchell et al. (2004) reported higher PWV values in men than in women.
On the other hand, studies exist, (London et al. 1995, Smulyan et al. 2001) which did not find a difference in PWV values between men and women.

1.2.3. Arterial Stiffness and Physical Exercise

When some kind of physical exercise, like endurance training or resistance training, is done over a certain period of time and when adaptation criteria, like intensity, load or extend, are fulfilled, the organisms shows signs of adaptation. Furthermore, acute responses, during and after physical exercise, can be observed and are in fact necessary in order to maintain a certain physical task and to stimulate longer term adaptation. These mechanisms of adaptation range from molecular and neurological to mechanical adaptations. During an acute exercise, for example, the increase in arterial pressure and shear stress stimulates the local release of growth factors which promote an increase in elasticity and distensibility in the central arteries (Prior et al. 2004).

Within the following chapters current knowledge and facts regarding the influences and/or adaptations of resistance training and endurance training on the arterial stiffness shall be presented.

1.2.3.1. Resistance Exercise

Resistance exercise is an accepted strategy to prevent sarcopenia-related functional impairment and osteoporosis as well as to increase muscle mass and muscle strength and is recommended by major health organisations for health promotion and disease prevention (Pollock et al. 2000, Miyachi et al. 2004, Miyachi 2013).
Furthermore, resistance exercise training is able to provoke positive changes concerning cardiovascular risk factors, like a lowering of blood pressure, decreasing percent body fat and increasing basal metabolic rate and quality of life (Williams et al. 2007).
Because of the positive effects of resistance training regarding muscle-loss and muscular strength, but also because some studies have shown positive effects of resistance training on the cardiovascular system, the American Heart Association has recommended the use of resistance training for the prevention and treatment of cardiovascular diseases (Haskell et al. 2007).

Though, passed studies have shown that resistance training might have negative effects on vascular function and arterial stiffness (Miyachi et al. 2004, Heffernan et al. 2007b, Collier et al. 2010).

In contrast to endurance training, the effects of resistance training are not that consistent concerning the effects on arterial stiffness. Studies exist that have shown inverse relationships between PWV and muscle strength or decreases in arterial stiffness. Even negative relationships between arterial stiffness and resistance training or increases in arterial stiffness but also studies which have shown both or neither or no changes at all exist (Bertovic et al. 1999, Miyachi et al. 2004, Rakobowchuk et al. 2005, Casey et al. 2007, Cortez-Cooper et al. 2008, Kawano et al. 2008, Heffernan et al. 2009, Yoshizawa et al. 2009, Fahs et al. 2010).
Within these investigations, interventional studies as well as cross-sectional studies can be found. Furthermore, these studies differ in part considerably in their characteristics like intervention period, population or training protocol. Casey et al. (2007) stated, that the conflicting results of studies investigating connections between arterial stiffness and resistance training may be due to high intensity and high volume training protocols in contrast to moderate, average training protocols. Also, whether arterial stiffness parameters are

being measured in central or in peripheral arteries has to be considered and might be a reason for yet, uncertain and different results in corresponding interventions.

Not only as a consequence of regular resistance training but also acutely, directly after a resistance exercise, studies have shown an increase in arterial stiffness (Miyachi et al. 2004, DeVan et al. 2005, Heffernan et al. 2007a, Fahs et al. 2009).
Moreover, eccentric resistance training seems to increase arterials stiffness to a smaller extend than concentric resistance training (Okamoto et al. 2006).

Besides possible negative changes concerning the cardiovascular system, resistance training has also shown to result in positive alterations like improvements in vascular function or limb blood flow (Anton et al. 2006, Olson et al. 2006, Cohen et al. 2008, Heffernan et al. 2009).
In physical exercises in which combinations of resistance training and endurance training components can be found, like for example rowing, negative effects of a resistance training seems to be compensated by the favourable effects of the endurance component and even can decrease arterial stiffness (Cook et al. 2006). Similar results could be shown as a result of a cross training (Kawano et al. 2006). These data may speculate that the negative effects of strength based sports on arterial stiffness can be negated when combined and performed parallel with endurance sports and its positive effects on arterials stiffness (Kawano et al. 2006, Otsuki et al. 2007a).
Further, a home-based resistance training showed a reduction in brachial-ankle PWV in middle aged women (Okamoto et al. 2009).
High intensity resistance training has shown to increase arterials stiffness (Miyachi et al. 2004, Miyachi 2013), moderate intensity resistance training has shown no effects in older individuals (Cortez-Cooper et al. 2008, Yoshizawa et al. 2009) and in low intensity resistance training a reduction in arterial stiffness could be found (Okamoto et al. 2011).

Further studies have shown that during, immediately after and up to 30 min post a resistance exercise session, large, central arterial stiffness was increased (DeVan et al. 2005, Heffernan et al. 2007a, Collier et al. 2010).

After all, several studies have shown different results and effects on arterial stiffness. Nevertheless, since possible underlying mechanisms for increases in arterial stiffness due to resistance training are unknown, authors who found increases in arterial stiffness have certain theories.

It is assumed that changes in arterial stiffness are originated from changes in blood pressure. In contrast to, partly enormous pressure changes, up to 310/250mm Hg, during resistance exercises, in endurance training such changes are not found due to the fact, that large muscles are mainly used in a rhythmical manner (Yoon et al. 2010).

During a resistance training blood pressures can increase tremendously due to high load. Furthermore, the Valsalva manoeuvre is commonly used on resistance training. In a study by Heffernan et al. (2007c) it could be shown that PWV as well as central arterial stiffness was significantly increased in situations in which breath was held and the Valsalva manoeuvre was performed. During this manoeuvre intrathoracic and intraabdominal pressure increases and is propagated towards the aorta (Hamilton et al. 1936). The pressure also increases the pressure on the intracellular space and the vascular wall and therefore causes a fatigue of the elastin and, in a row, their fraction and further the replacement with collagen fibres (Armentano et al. 1991).

Although central systolic blood pressure and arterial stiffness were significantly increased, no changes were observed in the brachial artery immediately after a resistance exercise which suggests that the assessment of the central, aortic pressures might be of greater help evaluating the effects of resistance training in contrast to brachial pressures (Yoon et al. 2010).

As mentioned, the knowledge regarding resistance training and its effects on arterial stiffness are divers and do not show a uniform picture.

1.2.3.2. Endurance Exercise

Several studies have proven positive effects of regular endurance training on the cardiovascular system, improved cardiorespiratory fitness, reduced cardiovascular risk factors and reduced cardiovascular mortality (Thompson et al. 2003, Seals et al. 2008). Moreover, studies have shown positive effects of endurance training concerning a reduction in peripheral blood pressure but also in arterial stiffness in young as well as in older adults (Cameron & Dart 1994, Kelley & McClellan 1994, Tanaka et al. 2000, Kakiyama et al. 2005, Otsuki et al. 2006, Sugawara et al. 2006, Collier et al. 2008).
Some authors pointed out the clear evidence for structural remodelling of the central arteries due to endurance training (Schmidt-Trucksass et al. 1999, DeVan & Seals 2012, Green et al. 2012).
On the other hand, some authors have postulated, that improved endothelial function and a reduction in sympathetic tone, rather than structural changes and remodelling are, considering the short time required for adaptation, responsible for endurance training caused decreases in arterial stiffness (Martin et al. 1990, DeSouza et al. 2000, Melanson & Freedson 2001, Hautala et al. 2004).

Despite a majority of suchlike studies, there is also some evidence, which showed higher arterial stiffness as a consequence of endurance training. Vlachopoulos et al. (2010b) and Burr et al. (2014) showed higher arterial stiffness in marathon and ultra-marathon runners, suggesting, that long-term strenuous exercise may accelerate the atherosclerotic process. The values estimated by Vlachopoulos et al. (2010b) for PWV for example in marathon runners was 6.89m/s whereas for recreationally active controls was 6.33m/s.
In another study, the number of completed marathons was correlated with coronary artery calcification (Mohlenkamp et al. 2008).

Repetitive episodes of arterial shear stress are thought to be the main reason and stimulus for vascular adaptations as a result of endothelium-dependent remodelling. This might be the reason for increased arterial stiffness in long, exhausting endurance exercises as the shear stress, and the remodelling caused by it, is intensified (Tinken et al. 2010).

Furthermore, the endurance training dependent aerobic capacity is also correlated with arterial stiffness. Several authors (Vaitkevicius et al. 1993, Rerkpattanapipat et al. 2002, Bonapace et al. 2003) have shown a relationship between the VO_{2max} and the stiffness of the arteries. Similar results were also identified by Fei et al. (2005). Moreover, they also found a persistent, although not strong, relationship between the aortic wave velocity and the heart rate recovery, a fact, which this working group interpreted in regard to a possible physiological linkage of these two parameters.

1.3. Aerobic Fitness Parameters

Aerobic fitness is the capacity to accomplish endurance performances that mainly depend on aerobic metabolism. Aerobic fitness could also be defined as the ability of oxygen delivery to the muscles in demand in order to generate energy during exercise (Armstrong & Welsman 2007). Health status and especially cardiovascular health has proved to be influenced by aerobic fitness (Léger 1996).
Dynamic exercise causes an increase in cardiac output as well as in heart rate. Furthermore, a dilatation of the systemic vascular bed occurs. As a consequence of cardiac output and the resistance of the vasculature blood pressure rises or falls. Therefore blood pressure is able to help assessing the integrity of myocardial contractility, chronotropic competence and the dilatation of the peripheral arterioles. This is why blood pressure is routinely measured and monitored during any dynamic stress test (Alpert & Fox 1993).

The circulatory system but also the whole organism undergoes complex changes from condition at rest to exercise. Heart rate as well as ejection fraction increases, due to a decrease in vagal tone, and lead to an up to 3 - 5 fold elevated cardiac output and stroke volume depending on the degree of physical stress. This increase is necessary in order to supply the exercising muscles with sufficient oxygen and fulfil the functional, metabolic demands. This response is than followed by an increase in the sympathetic outflow to the heart and systemic blood vessels (Washington et al. 1994). During a certain exercise, the peripheral vessels dilate and cause a decrease in peripheral resistance which usually occurs to a lesser degree than the increase in cardiac output which is why systolic pressure increases with a mostly unchanged diastolic blood pressure. Deviations of these blood pressure characteristics during an exercise testing are widely recognized as not physiological and impairments of cardiac performance (Alpert & Fox 1993, Washington et al. 1994).

Besides several parameters, which all have proved clinical value, maximal oxygen consumption (VO_{2max}) is by far the most frequently asses one in exercise testing (Fei et al. 2005).
In various studies, VO_{2max} has proved to correlate significantly with arterial stiffness. Moreover, VO_{2max} is, at least in part, determined by the capability of the arteries to dilate, and as a result enable to increase the flow to the muscles in demand. In a study by Vaitkevicius et al. (1993) three different indexes of arterial stiffness, including

aortic PWV, showed to be inversely related to VO_{2max}, being strongest in individuals older than 70 years.
Other studies found out, that in healthy young individuals an increased aortic stiffness was correlated with lower VO_2 and therefore a reduced exercise tolerance (Cameron & Dart 1994, Chen et al. 1999). Similar results were found by Bonapace et al. (2003) who showed that aortic stiffness was an independent predictor of peak VO_2. As this relationship was independent of age, they suggested that, not the well-known age-related changes in aortic wall composition but other factors might reduce the distensibility of the aorta and as a result physical exercise performance. In a study by Rerkpattanapipat et al. (2002) exercise intolerance was correlated with an aortic distensibility reduction.

Another parameter to assess physical fitness capacity is the heart rate recovery (HHR). Studies have shown that, the faster the heart rate recovers after a physical exercise, the better trained or the fitter the individual is. Furthermore, an abnormally prolonged HHR subsequent to an aerobic exercise indicates a coronary artery disease and endothelial dysfunction (Diaz et al. 2001, Huang et al. 2004, Lipinski et al. 2004).
Not only in diseased individuals, but also in healthy conditions HHR is correlated with aerobic fitness and cardiovascular health (Cardus & Spencer 1967, Kostis et al. 1982, Darr et al. 1988). One factor that has been shown to strongly influence HHR is the parasympathetic tone, with higher parasympathetic activity resulting in higher influence on the HHR (Fei et al. 2005).
Even though the strength of the correlation between HHR and the aortic PWV in a study by Fei et al. (2005) was not robust, the relationship between these was significant, indicating some kind of physiologically linkage. Furthermore, as HHR is correlated with aerobic fitness, aerobic fitness is related to arterial stiffness and improvements in aerobic fitness may cause improved arterial compliance.

Fei et al. (2005) also showed, that resting heart rate was significantly correlated with aortic PWV. Heart rate at rest is also correlated with endurance training. Highly trained endurance athletes show reduced resting heart rates due to a decreased activity of the sympathetic nervous system but also due to increased size of the heart (Findeisen et al. 1980).

1.4. Physical Exercise Performance Diagnostics and Parameter in Children

Children, and to a lesser degree also adolescents, are no miniature adults but differ from the latter in their physical, cognitive, social and psychological status and therefore have to be treated differently (Tomassoni 1993). This is especially true for establishing physical performance capacity in children and adolescents. However, many of the exercise tests used for children and adolescents are similar to those of adults. Actually, exercise testing of children requires special consideration in the administration of the tests, the collection of the data but also the representation and the interpretation of the results (Docherty 1996).

Children's aerobic fitness is well documented and it was Robinson (1938) who first published laboratory investigations of boys' aerobic fitness almost 80 years ago. More than 60 years have passed since Astrand (1952) conducted pioneering studies of the aerobic fitness of boys and girls.
Nevertheless, there are still unanswered questions and controversy regarding the clarification of children's aerobic fitness for example in terms of the right performance test, the right protocol or the right physiological measures per se (Armstrong & Welsman 2007).

The basic principle and goal of a clinical exercise testing is to place the organism under physical stress in order to evaluate its functional limits and uncover possible deficiencies and abnormalities not evident in the resting state (Rowland 1993b).
Besides these, another major reason for exercise testing in children and adolescents is to collect data and gain a better understanding of growing up, maturation and physical activity and to profile changes from childhood to adolescence. Furthermore, exercise testings help us to understand acute and chronic effects of physical exercise and training programs on children and adolescents (Docherty 1996).

One or more of the following paediatric exercise testing indications might be the reason for performing an exercise testing in children and adolescents (Rowland 1993b, Docherty 1996):

- Evaluating cardiac and pulmonary functional capacity,
- detecting myocardial ischemia,
- evaluating cardiac rhythm and rate,
- determining blood pressure response,
- assessing symptoms with exercise,
- detecting and managing exercise-induced asthma,
- chartering the course of a progressive disease and evaluating therapy,
- assessing the success of rehabilitation programs,
- assessing physical fitness

as well as

- developing profiles that describe normal patterns of,
- understanding individual variation within,
- assessing impact of environmental factors on,
- assessing effects of regular physical activity on growth, maturation and physical performance.
- Examining trainability,
- understanding acute response to exercise and
- monitoring secular trends.

In children, in contrast to adolescents and adults, exercise testing is more challenging and difficulties in testing might occur to following reasons:

- Children's body size is small in relation to testing equipment,
- children's peak performance is relatively weak in contrast to the minimal work rate setting and
- children's shorter attention span, motivation and compliance.

Although first exercise testing protocols for children were originally developed for adults, today several protocols for children have been described in the literature with modifications for children and adolescents in increment time and intensity (Bar-Or

1993, Freedson & Goodman 1993, Rowland 1993a, Léger 1996). Some protocols even intend adaptations regarding body weight and body height (Léger 1996).
One of the most common used protocols is the Bruce treadmill protocol, originally developed for adults but nowadays used for children from the age of 4 years all over the world (Bruce et al. 1973, Wessel et al. 2001).
Nevertheless, it depends on the individual, the research question and the equipment which protocol is used (Hebestreit 2004).
From 6 years of age, most children will be able to complete standardized treadmill as well as cycle ergometer protocols (Hebestreit 2004).
Due to the risk of premature muscle fatigue, total exercise time should be between 6 - 10 minutes and protocols with shorter increment time are preferred when conducted to measure individuals performance (Hebestreit 2004).

The most commonly used devices for paediatric exercise testing are the cycle ergometer and the treadmill (Tomassoni 1993). Both have advantages and disadvantages regarding function, costs and organisation as well as in validity and implementation.
In order to choose between the cycle ergometer and the treadmill, four considerations should be made (Washington et al. 1994):

- How much space is available for the exercise laboratory?
- What is the size of the subjects?
- What are the reasons for the exercise testing?
- What and how many parameters are going to be monitored and recorded?

The request, that paediatric researches should not be fixated with exercise testing protocols and approaches that are routinely used for adults, became louder in recent years (Rowland 1996). Instead, they should watch out for how children actually exercise in real life (Cooper 1995).
In young children, approximately up to the 7^{th} year of age, some authors declare themselves in favour of performing treadmill testings and not cycle ergometer testings due to the children's relatively undeveloped knee extensors (Bar-Or & Rowland 2004).

Normative data for age, gender and body size, as well as standard values and reference values for common outcome variables, like for example VO_{2max}, ventilatory

or lactate threshold, in exercise testing in healthy children are available for several exercise protocols (Hebestreit 2004).

The VO_{2max} values on a cycle ergometer are on average 7 - 19% below the VO_{2max} values on a treadmill. These differences depend not only on the device but also on the individual and the testing protocol (Léger 1996).
High values of VO_{2max} indicate a powerful well-functioning cardiovascular system which is able to accomplish submaximal loads with less fatigue.
In adults, a levelling-off or plateau of the VO_2 measurement values despite increasing intensity is a conventional criterion for approaching the $VO_{2max.}$ This is less pronounced in children (Léger 1996) and was first described by Astrand (1952).
During puberty VO_{2max}/kg slightly decreases in girls whilst staying almost the same in boys. This can be explained by the increasing body fat in girls during this age. Furthermore, the maximal O_2 consumption is correlated with the lean-body-mass and when expressed regarding muscle mass these gender-related differences almost disappear (Bar-Or 1986). Additionally, in trained girls VO_{2max}/kg remains the same whilst in boys it increases (Léger 1996). Rowland (1993a) reported, that maximal power output in growing boys is 3.5 Watt/kg and in growing girls is 3 Watt/kg.
Absolute VO_{2max} systematically increases during growth as it is higher in larger individuals and as it is proportional to the active muscle mass (Léger 1996).

Whilst intra-individual changes in aerobic capacity are better compared with absolute VO_{2max}, inter-individual comparisons of the aerobic capacity are better done with VO_{2max}/kg lean-body-mass (Léger 1996).

The heart rate in adults usually increases linearly with the rate of work in dynamic exercises. As children have smaller hearts and as a result smaller cardiac output, due to their smaller bodies, their system compensates this fact with an increased heart rate which is why children show higher maximal heart rates than adults (Washington et al. 1994).
Although the peak exercise heart rate can be an indicator for the degree of the exhaustion in adults as well as in children, large inter-individual differences have to be considered (Rowland 1993a).
Furthermore, when measuring blood pressure it should also be considered, that systolic blood pressure at maximal exercise is dependant of the body size (Alpert et al. 1982).

1.5. Relevance, Question and Hypothesis

The quantification of arterial stiffness parameters (PWV and AIx) is quite controversial and the development of reference values is a topic of some discussion as there has not been a widely accepted consensus on such values.

Although one can find some descriptions of reference values in the literature, they are scarce and differ from literature to literature. This is even more the case in adolescents and especially the case in children were only a few reference values can be found yet.

The ongoing need for normative and reference values for specific arterial stiffness measurement devices has been postulated by several studies which have compared several different PWV measuring devices (Khoshdel et al. 2006, Pannier et al. 2002, Rajzer et al. 2008). Moreover, reference values and/or threshold values for elevated PWV for different populations, like children, adults, elderly, healthy, diseased and athletes have to be confirmed and fixed, as, for example, the results of Merrill et al. (2011) indicate the limitation of a focus on only one single clinically significant fixed threshold value.

In a study by Voges et al. (2012) reference values for aortic PWV in children and young adults by means of CMR (cardiovascular magnetic resonance) were established. They showed an increase of PWV with age as well as in arterial stiffness. An age-dependent increase in arterial stiffness has also been reported by other authors (Avolio et al. 1983, Senzaki et al. 2002). Nevertheless, an uniform opinion on and/or uniform reference values for arterial stiffness at rest are scarce and for post exhaustion do not even exist in children. Therefore, one aim of this study was to assess reference values of arterial stiffness at rest in young physically active males.

During the process of physical exercise the cardiovascular system undergoes, like most systems of the organism, different, partially dramatic, changes.

To our knowledge no data exist concerning the range of the adaptability of arterial stiffness. If a higher adaptability of arteries' elasticity, expressed as a wider physiological range of arterial stiffness, was associated with higher physical performance capacity, arterial stiffness and an easy to conduct PWV measurement could be used in order to assess ones performance capacity. Hence, another aim of this study was to assess post exhaustion arterial stiffness values and to assess the physiological ranges and the adaptability of arterial stiffness between rest and exhaustion in this group of participants.

Our hypothesis is that, similar to other parameters of the cardiovascular system, the arteries and the arterial stiffness per se experiences alterations in stiffness as an answer to physical exercise. Furthermore, we hypothesize that these alterations are dependent of the physical performance capacity and that the better trained one is the higher is the possible physiological range of central arterial stiffness. Another hypothesis is that in children, like in adults, PWV values are decreased in comparison with non-athletes as a result a regular physical training.

Taken together these facts, this study was conducted with the following aims in order to verify our hypotheses:

1. To ascertain PWV and AIx reference values in young, healthy, male soccer players aged 8 - 18.

2. To identify whether these values change and/or differ during the process of aging in this population.

3. To ascertain post physical exhaustion exercise PWV and AIx values in this population.

4. To identify whether these values change and/or differ during the process of aging in this population.

5. To identify possible correlations between the Pre- and Post- exercise PWV and AIx values in this population.

6. To identify whether these correlations change and/or differ during the process of aging in this population.

7. To identify possible correlations between Pre- and/or Post- exercise PWV and AIx values and the physical performance capacity in this population.

8. To identify whether these correlations change and/or differ during the process of aging in this population.

2. Material and Methods

All interventions, measurements and the acquisition of the data took place at the Austrian Institute of Sports Medicine (ÖISM, Österreichisches Institut für Sportmedizin) at the Centre of Sports Science and University Sports (ZSU, Zentrum für Sportwissenschaften und Universitätssport) of the University of Vienna, Auf der Schmelz 6, 1150 Wien, within 3 months from October 2013 to December 2013.

2.1. Participants

The soccer players were all members of the youth squad of a famous Vienna soccer club playing in the Austrian Soccer League.
To be included in the study, subjects had to meet certain criteria.
Out of 179 recruited individuals a total of 173 healthy, young (8 - 18 years), male soccer players has been tested in this study, while 6 individuals had to be turned down due to one or more of the following exclusion criteria:

- Body height < 120cm
- Acute illness or less than 3 weeks ago
- Acute injury/operation or less than 2 months ago
- With medication
- History of, or acute cardiovascular, metabolic, pulmonary or orthopaedic disease

Only currently healthy subjects, without any medication intake, with no history of cardiovascular, metabolic, pulmonary, orthopaedic, or any other diseases affecting cardiovascular parameters and workload capacity in any way, were allowed to participate. Currently or recently (within the last three weeks) ill and currently or recently (within in the last two months) operated or injured subjects were excluded.
Out of this total of 173 participants 7 did not finish the ergometry to exhaustion due to different reasons like muscle pain, nausea or the lack of skill to ride the ergometer and therefore slipping out of the pedals. The last one was especially the case in the youngest group of participants. Furthermore, in another 50 out of these 173 subjects we were not able to measure certain post-ergometry to exhaustion parameters, due to certain measurement problems with the arterial stiffness measurement device, which makes a final total of 116 individuals from whom we were able to receive all

measured parameters. Nevertheless, we used the mentioned 57 individuals from whom no post ergometry to exhaustion data could be gained, together with the 116 “full-parameter-subjects” for other analysis like analysis of pre ergometry to exhaustion data.

The finally participating subjects were, according to the common youth squads of this soccer club, divided into 5 groups which, with one exception, represented participants within 2 years of age, respectively. The oldest group represented participants within 3 years of age (Table 3).

Table 3: Description of the corresponding age - Age-groups.

Age of participants (years)	Age-group	n
8 - 9	U10	14
10 - 11	U12	36
12 - 13	U14	39
14 - 15	U16	47
16 - 18	U18	37

The participants were recruited as the ÖISM is the sports medical and exercise physiological partner of this soccer club and therefore the players of the squads regularly undergo physical and medical testings at the ÖISM.
All participants received instructions for the medical measurements as well as for the ergometry to exhaustion and the arterial stiffness measurement and were able to familiarize themselves with the protocol.
All participants had their tests in the forenoon in two different examination rooms. In one room the medical preliminary assessment and in the other the ergometry and the arterial stiffness measurements took place. According to the guidelines for ergometries (Wonisch et al. 2008) both rooms were controlled for temperature at 20°C, a relative air humidity of 30 - 60% and sufficient lamination and ventilation. Participants were asked to have breakfast and something to drink on the day of their tests and not to eat anything by no later than 1 hour before the testing. They also were asked to withstand caffeine that day and heavy physical activity and alcohol the day before their testing.

A letter of agreement had to be signed by the participants' parents or, in the case of being authorised to sign, by the participant himself and all participants took part voluntarily.

Anthropometric measurements, physiological measurements the conduction of the ergometry to exhaustion as well as the arterial stiffness measurements were all performed and supervised by trained and professional sports scientists or members of the medical staff of the ÖISM.

2.2. Medical Preliminary Assessment

In combination with the inclusion and exclusion criteria, a medical preliminary assessment was done by a member of the medical staff of the ÖISM on the participants to find out about any acute impairments to health. Therefore a standardized internistic, orthopaedic and sport medical testing was done which included an anamneses questionnaire, an orthopaedic assessment, an electrocardiogram (ECG), a stethoscopic monitoring and the assessment of body weight, body height and the blood pressure.

2.3. Anthropometric Parameters

Table 4 shows the anthropometric data of all in this study tested und processed participants. Within these parameters data was ascertained as follows:

2.3.1. Body Weight

Bodyweight was measured in kg with a precision electronic scale (Seca, Type 754) with an accuracy of 0.5kg. For the measurement the participants had to take off all clothes except their underwear. Also, watches, rings, necklaces and suchlike had to be taken off.

2.3.2. Body Height

Body height was measured in meters by a fixed stadiometer (Seca) with an accuracy of 1cm. For the measurement the participants had to take off their shoes and socks, standing upright and backwards to the wall looking straight ahead.

2.3.3. Body Mass Index (BMI)

The BMI was calculated automatically with an accuracy of one decimal place by the following formula:

BMI = m (body weight in kg) / l (body height in m^2)

Subjects' BMI was compared to reference values for Boys 5 to 19 years by the World Health Organization (WHO) (http://www.who.int/growthref/who2007_bmi_for_age/en/ ; z-scores: boys, pdf; access on the 21.05.2014).

2.3.4. YUG-SY

The distance between the pubic symphysis and the sternal notch (jugulum) was measured by a medical measuring tape (Seca) in supine position in cm with an accuracy of 1cm. Both, the symphysis as well as the jugulum were palpated on the naked skin and the measuring tape was stretched between this points, paying attention that the tape did not touch the body surface which could have meant measuring inaccuracy.

The YUG-SY distance is needed by the arterial stiffness measurement software in order to calculate the PWV and the AIx. In a study by Sugawara et al. (2008) superficial measurement of aortic length has proved to be rather close to the true aortic length.

Table 4: Subject characteristics of all (Total; n = 173) subjects and within the groups.

Parameter	Age-groups	Statistic
Age (y)	U10	9 (8 - 9)
	U12	11 (10 - 11)
	U14	13 (12 - 13)
	U16	14 (14 - 15)
	U18	17 (16 - 18)
	Total	13 (8 - 18)
Height (m)	U10	1.35 (1.27 - 1.47)
	U12	1.45 (1.29 - 1.60)
	U14	1.60 (1.41 - 1.77)
	U16	1.73 (1.59 - 1.85)
	U18	1.79 (1.65 - 1.89)
	Total	1.65 (1.27 - 1.89)
Weight (kg)	U10	29.5 (26 - 35)
	U12	35 (24 - 44)
	U14	45 (34 - 70)
	U16	61 (48 - 80)
	U18	70 (59 - 83)
	Total	52 (24 - 83)
BMI (kg/m2)	U10	16.3 (15 - 18.1)
	U12	16.6 (13.7 - 20.1)
	U14	17.8 (15.2 - 24.2)
	U16	20.4 (16.7 - 24.7)
	U18	22.0 (19.4 - 25)
	Total	18.8 (13.7 - 25)

Note: Data expressed as median (minimum - maximum).

2.4. Physiological Parameters

2.4.1. Blood Pressure (BP)

BP was measured by the arterial stiffness measurement software before and after the ergometry to exhaustion. In the course of the medical preliminary assessment and during the ergometry to exhaustion, BP, as a matter of medical supervision, was measured by hand (ERKA, Perfect Aneroid).

2.4.1.1. Systolic Aortic Blood Pressure (SBPao)

SBPao was measured by the arterial stiffness measurement software before and after the ergometry to exhaustion.

2.4.2. Pulse Pressure (PP)

Peripheral, brachial PP was measured by the arterial stiffness measurement software before and after the ergometry to exhaustion. The PP is defined as the difference between the systolic and the diastolic pressures.

2.4.3. Mean Arterial Pressure (MAP)

Peripheral, brachial MAP was measured by the arterial stiffness measurement software before and after the ergometry to exhaustion. The MAP is defined as the average arterial pressure during a single cardiac cycle.

2.4.4. Heart Rate (HR)

HR was measured by the arterial stiffness measurement software before and after the ergometry to exhaustion. During the test pulse was measured by means of the ECG.

2.4.5. Arterial Stiffness Parameters (PWV, AIx)

Both parameters, the pulse wave velocity (PWV), as well as the augmentation index (AIx) were measured by the Arteriograph (TensioMed, Budapest, Hungary; Software Arteriograph 3.0.0.1 for Windows 7). This device measures PWV and AIx by analysis of the oscillometric pressure curves on the upper arm by a special high fidelity sensor. The arterial stiffness measurement of the Arteriograph is based on the fact that the blood volume being ejected into the aorta during systole generates a pulse wave. This pulse wave is then reflected on bifurcations. The time delay between the beginning of the first pressure wave and the beginning of the reflected second pressure wave is put in relation to the before measures distance from pubic symphysis and the sternal notch resulting in the PWV in m/s.

Therefore the cuff is inflated two times. Initially it measures BP after which the device produces a cuff pressure 35mm Hg above the measured systolic BP and therefore completely occludes brachial artery. Now the pressure fluctuations in the brachial artery can be detected. These cuff information are recorded and analysed by the computer software. The measurement itself, from fixing the arm cuff until the result of the measurement lasts 2 - 3 minutes.

The midarm circumference of the left arm was measured and the according cuff was adapted (small: 18 - 25cm, medium: 26 - 33cm, large 34 - 43cm).

The arterial stiffness measurement was immediately done after the medical preliminary assessment in supine position. Participants were told to relax and close their eyes for 10 minutes, during which patient data were entered and the midarm and the YUG-SY distances were measured, before the testing.

The technical validity of this device has been confirmed previously in hypertensive, non-hypertensive and treated hypertensive adults (Baulmann et al. 2008, Rajzer et al. 2008, Jatoi et al. 2009).

2.4.5.1. PWV

The PWV is defined as the speed at which a pulse wave moves through an arterial segment (Oliver & Webb 2003). In dependence in which arterial segment of the body PWV is measured, central or aortic PWV (cPWV, aoPWV) can be distinguished from for example brachial-ankle PWV. Even though PWV can be measured in any arterial segment measurement of the

aoPWV is considers to be the “gold-standard” in non-invasive measurements (Laurent et al. 2006).

2.4.5.2. AIx

AIx is calculated as the ratio between the augmented central pressure, due to reflected waves (AP), and pulse pressure (PP) and is described in percent (Salvi & Parati 2012), AIx (%) = AP/PP.

The blood volume ejected into the aorta by the left ventricle during systole generates a forward pressure wave. This forward wave is reflected along the arterial tree as a result of decreasing diameter of the arteries and impedance mismatch. The sum of these two pressure waves is the arterial pulse wave. The reflected pressure wave augments the first pressure wave (augmentation pressure) and the time point at which these two pressure waves merge as well as the amplitude of the reflected wave affects the aortic blood pressure. AIx is defined as the ratio of the amplitude of the late systolic peak to the amplitude of the first/early systolic peak (Shimizu & Kario 2008, Weber 2010, Hughes et al. 2013).

In dependence in which arterial segment of the body the AIx is measured, central or aortic AIx (AIxc, AIxao) can be distinguished from brachial-ankle AIx (AIxba).

2.4.5.3. ∆PWVao and ∆AIxao

The difference between the parameter values for PWVao and AIxao, respectively, before and after the cycle ergometer stress test were defined as ∆PWVao and ∆AIxao. These values represent the magnitude of change within these parameters between the Pre and Post measurements. The larger the ∆ value, the larger the change and the difference between the measurement before and after the ergometry.

2.5. Parameters of Endurance Capacity

The exercise to exhaustion was done on a cycle ergometer (IEC 60 - 1-60, Type 911905, by Lode B. V. medical Technology, Groningen, Netherlands). The used software for the Watt-control was Excalibur III by Lode medical Techonology and the software for the ECG exercise test was Sema-200 2.43 by Schilla AG. In order to assess the participants' maximal workload during the ergometry to exhaustion the Watts, defined as an amount of energy conversion per period of time, where calculated.

Maximal power output was calculated as follows:

$$\mathbf{W_{max} = WE + (40W/t \times tE)}$$

W_{max} = maximal power output (watts), WE = power output of last complete stage (watts), 25W = workload increment, t = workload duration (seconds), tE = duration of final stage (seconds).

In the course of the test to exhaustion the heart was monitored by ECG, from which the heart rate was gained, too. Moreover blood pressure was measured every two minutes by hand.
The subject sat on the ergometer at an optimal saddle height (Peveler et al. 2007). Pedal baskets were used to avoid losing the pedals and to assure maximal force transmission. The participants had to stay seated on the saddle throughout the test. A 5-minute warm-up period at the level of one Watt (W) / kg body weight at 70 - 80 rpm was performed prior to the test, but the subjects were given a 1 minute rest before the beginning of the tests.
All participants started with a workload of 1 Watt/kg body weight which was increased every minute by 25 Watts. A cadence of 70 - 100 had to be maintained. As soon as the participants gave up, due to exhaustion, the measurement was stopped, the person lied down on the examination bed and the arterial stiffness measurement was started. Due to this position change and the measuring time of the arterial stiffness software, results were gained approximately 3 minutes after the ergometry break-up. Therefore the gained arterial stiffness parameters do not exactly represent the situation at the maximum exhaustion but the one 2 - 3 minutes afterwards. This mend, that the arterial stiffness measurement took place on average at 67% of the

maximal heart rate (Table 6). Due to the software's calculation this could not be prevented and had to be considered.

2.6. Statistics

All statistical analysis were performed using SPSS (IBM SPSS Statistics, Version 22, Chicago, IL, USA).

All data were tested for normal distribution with the Kolmogorow-Smirnow test for normality.

Differences between Pre and Post values over the whole study population were assessed with Wilcoxon test.

In order to analyse Pre and Post data, respectively, between the groups U10, U12, U14, U16 and U18, univariate analysis of variance (ANOVA) was used.

ANOVA with repeated measures were used to evaluate changes in Pre and Post parameters data between the different age-groups. When a statistically significance in group-by-time interaction and/or within-group comparison and/or between time points were observed, Bonferroni Post-hoc analysis was performed.

The quantitative data were expressed as median, minimum and maximum or mean value, standard deviation and minimum, maximum, depending on the used test.

Spearman-Rho coefficients were detected to reveal potential correlations between parameters of arterial stiffness and parameters of physical performance over all groups as well as within the age-groups. A p-value of < 0.05 was considered as being statistically significant.

3. Results

The participating subjects were, according to the youth squads of the soccer club, divided into five age-groups. The data received from this study were analysed within these groups but also over all participants.

3.1. Descriptive Statistics

Within this chapter the ascertained values for heart rate, blood pressures, Watts and arterial stiffness parameters (PWV, AIx) are presented.

3.1.1. Heart Rate

In all groups HR_{max} was around 190 and the HR after the ergometry (HR Post) was in all groups higher than the HR before the exhaustion (HR Pre) (Table 5).
The HR Pre tended to decrease in the groups with increasing age (-groups) whilst the HR Post tended to increase.
As the HR measured during the arterial stiffness measurement after the ergometry took place approximately 2 - 3 minutes after the ergometry was finished, the HR Post is not correspondent to the maximal HR. In fact, the HR Post was on average 67% of the HR_{max}, due to the delayed measurement time point. Table 6 shows the average percentages, as well as the minimum and maximum percentages of the HRs at the time point of the arterial stiffness measurement in the different groups and over all subjects.

Table 5: Heart rate previous (HR Pre) and after (HR Post) the ergometry, as well as the maximal HR (HR_{max}) in the groups and over all groups.

Group	Parameter		
	HR Pre (n=173)	**HR_{max} (n=172)**	**HR Post (n=166)**
U10	73 ± 9.6	187 ± 9.6	99 ± 21.4
U12	69 ± 10.6	190 ± 8.8	121 ± 22.8
U14	70 ± 10.7	194 ± 7.6	139 ± 16.5
U16	64 ± 9.4	193 ± 7.8	132 ± 18.2
U18	60 ± 7.5	191 ± 7.1	135 ± 15.9
Total	65 ± 10.4	192 ± 8.1	130 ± 21.3

Note: Data expressed as mean value ± standard deviation. Heart rate (HR) in beats/minute.

Table 6: Min., max. and mean value of the HR Post in percentage of the HR_{max} in the groups and over all groups.

Group	Minimum (%)	Maximum (%)	Mean value (%)
U10 (n=14)	38	70	53.71 ± 10.13
U12 (n=34)	35	77	63.16 ± 10.80
U14 (n=37)	58	85	71.21 ± 6.81
U16 (n=44)	46	87	68.28 ± 8.74
U18 (n=37)	49	87	70.19 ± 6.77
Total (n=166)	35	87	67.08 ± 9.81

Note: Date expressed as mean value ± standard deviation. Heart rate (HR) in beats/minute.

3.1.2. Blood Pressures

Table 7 shows the values of all blood pressure parameters (systolic pressure, diastolic pressure, mean arterial pressure, pulse pressure, systolic aortic pressure) before (Pre) the ergometry in the different groups and over all participants, whilst table 8 shows the blood pressure parameter values after the ergometry (Post).

Table 7: Blood pressure parameters before the ergometry in the groups and over all groups.

Group	Parameter Pre				
	SBP	**DBP**	**MAP**	**PP**	**SBPao**
U10 (n=14)	117 (100 - 129)	60 (51 - 70)	75 (69 - 90)	57 (41 - 69)	99 (91 - 114)
U12 (n=36)	113 (97 - 149)	60 (47 - 81)	78 (67 - 104)	51 (40 - 73)	101 (84 - 130)
U14 (n=39)	125 (111 - 189)	69 (55 - 91)	87 (74 - 108)	56 (41 - 121)	110 (94 - 192)
U16 (n=47)	127 (109 - 185)	67 (50 - 97)	86 (70 - 126)	62 (45 - 88)	111 (92 - 162)
U18 (n=37)	127 (108 - 146)	68 (46 - 83)	86 (67 - 102)	58 (44 - 81)	110 (93 - 141)
Total (n=173)	124 (97 - 189)	66 (46 - 97)	85 (67 - 126)	57 (40 - 121)	108 (84 - 192)

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Data expressed as median (minimum - maximum).

Table 8: Blood pressure parameters after the ergometry in the groups and over all groups.

Group	Parameter Post				
	SBP	**DBP**	**MAP**	**PP**	**SBPao**
U10 (n=14)	138 (115 - 156)	68 (53 - 75)	90 (76 - 102)	72 (56 - 86)	113 (98 - 155)
U12 (n=34)	152 (124 - 194)	78 (55 - 111)	103 (79 - 139)	73 (51 - 91)	122 (92 - 165)
U14 (n=37)	164 (127 - 207)	85 (61 - 103)	107 (89 - 138)	80 (44 - 104)	114 (94 - 175)
U16 (n=44)	173 (142 - 233)	79 (58 - 133)	110 (87 - 166)	95 (71 - 115)	139 (104 - 206)
U18 (n=37)	173 (145 - 209)	77 (59 - 106)	108 (88 - 139)	97 (72 - 134)	136 (99 - 170)
Total (n=166)	164 (115 - 233)	77 (53 - 133)	106 (76 - 166)	84 (44 - 134)	127 (92 - 206)

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Data expressed as median (minimum - maximum).

Table 9 shows the participating subjects divided into groups of 8 - 15 years of age and 16 - 18 years of age. The number of subjects and the corresponding percentages within these groups are listed for the blood pressure states according to the blood pressure reference values of the “Deutsche Hochdruckliga – Deutsche Gesellschaft für Hypertonie und Prävention” (http://www.hochdruckliga.de/blutdruckwerte-von-kindern.html, access on the 21.05.2014). 31.6% of the under 16 years old subjects were with normotone systolic as well as diastolic blood pressure values whilst the other 68.4% were at least in the systolic or in the diastolic blood pressure at least high normotone. In the group of 16 - 18 years old participants, 40.5% had both blood pressure parameters normotone in contrast to 59.5% who had at least one high normotone blood pressure value. All of the 16 - 18 years subjects had a normotone diastolic blood pressure.

Table 9: Systolic and diastolic blood pressures of the participating subjects according to the blood pressure reference values for children by “Deutsche Hochdruckliga – Deutsche Gesellschaft für Hypertonie und Prävention” (http://www.hochdruckliga.de/bluthochdruck.html, access on the 21.05.2014).

Blood Pressure		Age (Years)	
		8 - 15 (n=136)	16 - 18 (n=37)
Systolic	normotone	55 (40.4%)	15 (40.5%)
	high normotone	31 (22.8%)	13 (35.1%)
	hypertension	50 (36.8%)	9 (24.4%)
Diastolic	normotone	104 (76.5%)	37 (100%)
	high normotone	15 (11.0%)	0 (0%)
	hypertension	17 (12.5%)	0 (0%)
Systolic and Diastolic normotone		43 (31.6%)	15 (40.5%)

In children and adolescents, it is uncommon to define reference and threshold values for blood pressure due to the fact that suchlike are senseless because of growing and fast changing bodies as well as possible huge differences in physical maturation and development at the same age. As a result, blood pressures of children and adolescents are most commonly compared to percentile limits

according to factors that show the strongest influence on blood pressure, like body height and age.

Table 10 shows estimated percentiles for of blood pressure according to age and age-groups, respectively, of the population of this study. For certain ages and age-groups no percentiles could have been estimated, illustrated as "-".

Table 10: Representation of the percentile limits for systolic and diastolic blood pressure of the participants of this investigation by age and age-groups.

Age-group	Age		Percentiles						
			5%	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**
U10 (n=14)	8 (n=6)	Systolic	102	102	108	114	121	**-**	**-**
		Diastolic	51	51	51	57	62	**-**	**-**
	9 (n=8)	Systolic	100	100	106	116	128	**-**	**-**
		Diastolic	54	54	55	61	64	**-**	**-**
U12 (n=36)	10 (n=17)	Systolic	97	99	106	110	118	**124**	**-**
		Diastolic	47	53	58	60	65	**72**	**-**
	11 (n=19)	Systolic	101	101	106	113	120	**142**	**-**
		Diastolic	50	51	54	59	67	**79**	**-**
U14 (n=39)	12 (n=18)	Systolic	111	114	118	122	130	**136**	**-**
		Diastolic	57	60	62	66	70	**72**	**-**
	13 (n=21)	Systolic	111	113	123	126	137	**146**	**185**
		Diastolic	55	56	65	70	75	**78**	**90**
U16 (n=47)	14 (n=30)	Systolic	110	116	120	126	137	**143**	**168**
		Diastolic	51	52	62	68	72	**78**	**87**
	15 (n=17)	Systolic	114	116	124	128	131	**139**	**-**
		Diastolic	55	55	60	62	71	**79**	**-**
U18 (n=37)	16 (n=11)	Systolic	112	113	118	124	132	**144**	**-**
		Diastolic	53	54	60	66	73	**76**	**-**
	17 (n=24)	Systolic	109	112	118	130	137	**141**	**145**
		Diastolic	48	54	60	68	73	**76**	**81**
	18 (n=2)	Systolic	114	114	114	121	-	**-**	**-**
		Diastolic	64	64	64	72	-	**-**	**-**

Note: Due to the little "n" in certain ages, no 90th, 95th or 75th percentile could be estimated. Age in years, percentiles of blood pressure values in mm Hg.

3.1.3. Watt

Whilst the absolute Watt, achieved by the participants, increase with increasing age in the age-groups, the Watt/kg were similar in the different groups (Table 11). When analysed for statistically significance the following results were detected: Whereas in absolute Watt, differences between each of the groups could be found (U10: U12 (p=0.006), between each of the others p=0.000) this was not the case for Watt/kg. In Watt/kg differences between the youngest group, the U10, and the U12 (p=0.045), U14 (p=0.022) and the U18 (p=0.017), but not between the U10 and the second oldest group, the U16, could be found (Table 11).

Table 11: The achieved Watt and Watt/kg in the groups and over all groups.

Group	Parameter	
	Watt	**Watt/kg**
U10 (n=14)	127.0 (85 - 154)	4.30 (3.1 - 4.9)
U12 (n=36)	158.0 (107 - 228)	4.64 (3.2 - 5.9)
U14 (n=39)	205.0 (155 - 300)	4.62 (3.6 - 5.5)
U16 (n=47)	279.5 (197 - 352)	4.46 (2.9 - 5.5)
U18 (n=37)	316.0 (262 - 402)	4.69 (3.7 - 5.6)
Total (n=173)	233.5 (85 - 402)	4.60 (2.9 - 5.9)

Note: Data expressed as median (minimum - maximum).

3.1.4. Arterial Stiffness Parameters (PWV, AIx)

In all groups and over all groups, PWVao values showed higher levels after the ergometry than before the ergometry and on average almost doubled (Table 12). Aortic augmentation index did not show a different, that clear development. In contrast to the values of AIxao before the ergometry which showed to decrease with increasing age (-group), values of the AIxao after the ergometry did not show a constant development (Table 12).

Table 12: Parameter values of PWVao and AIxao, respectively, before (Pre) and after (Post) the ergometry in the different groups and over all subjects.

Group	Parameter			
	PWVao Pre	**PWVao Post**	**AIxao Pre**	**AIxao Post**
U10	5.3 (4.4 - 5.7)	5.9 (5.0 - 14.2)	10.30 (2.4 - 24.4)	5.30 (-1.3 - 32.5)
U12	5.3 (4.5 - 6.5)	7.3 (5.1 - 13.8)	13.40 (4.8 - 27.9)	7.30 (-12.3 - 84.8)
U14	5.7 (4.7 - 8.0)	10.7 (6.0 - 18.5)	5.25 (-3.4 - 35.2)	13.75 (-10.8 - 85.3)
U16	5.9 (4.9 - 10.7)	12.4 (6.2 - 19.3)	5.20 (-4.2 - 35.7)	2.70 (-6.0 - 84.3)
U18	6.2 (4.9 - 18.0)	12.8 (7.4 - 18.7)	1.95 (-3.2 - 44.1)	4.70 (-5.8 - 83.9)
Total	5.6 (4.4 - 18.0)	10.3 (5.0 - 19.3)	7.20 (-4.2 - 44.1)	6.20 (-12.3 - 85.3)

Pulse wave velocity aortic (PWVao) in m/s, augmentation index aortic (AIx) in %.
Note: Data expressed as median (minimum - maximum).

3.2. Differences

Differences in certain parameters between the groups, between Pre and Post ergometry values as well as differences in changes of parameter values between groups are described and illustrated in this chapter.

3.2.1. Differences in Parameters between Pre and Post Values over all Groups

Differences (p=0.000) between the Pre and the Post values over all participants were found for the following parameters: PWVao, HR, SBP, DBP, MAP, PP and SBPao. No differences between Pre and Post values over all participants were found in the aortic augmentation index (p=0.472) (Table 13).

As Figure 12 shows, values of all measured blood pressures as well as the HR increased from Pre to Post ergometry measurements. In arterial stiffness parameters, PWVao showed increased values after the ergometry, in contrast to AIxao which showed a decrease from Pre to Post.

Table 13: Median of parameters prior (Median Pre) and after (Median Post) the ergometry as well as the statistically significance (p-value).

Parameter	Median Pre	Median Post	p-value
PWVao	5.6 (4.4 - 18)	10.3 (5.0 - 19.3)	0.000
AIxao	7.20 (-4.2 - 44.1)	6.20 (-12.3 - 85.3)	0.472
HR	65.0 (43 - 103)	130.0 (66 - 176)	0.000
SBP	124 (97 - 189)	164 (115 - 233)	0.000
DBP	66 (46 - 97)	77 (53 - 133)	0.000
MAP	85 (67 - 126)	106 (76 - 166)	0.000
PP	57 (40-121)	84 (44 - 134)	0.000
SBPao	108 (84 - 192)	127 (92 - 206)	0.000

Pulse wave velocity aortic (PWVao) in m/s, augmentation index aortic (AIxao) in %, heart rate (HR) in beats/minute, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Data expressed as median (minimum - maximum), Differences were detected using Wilcoxon test.

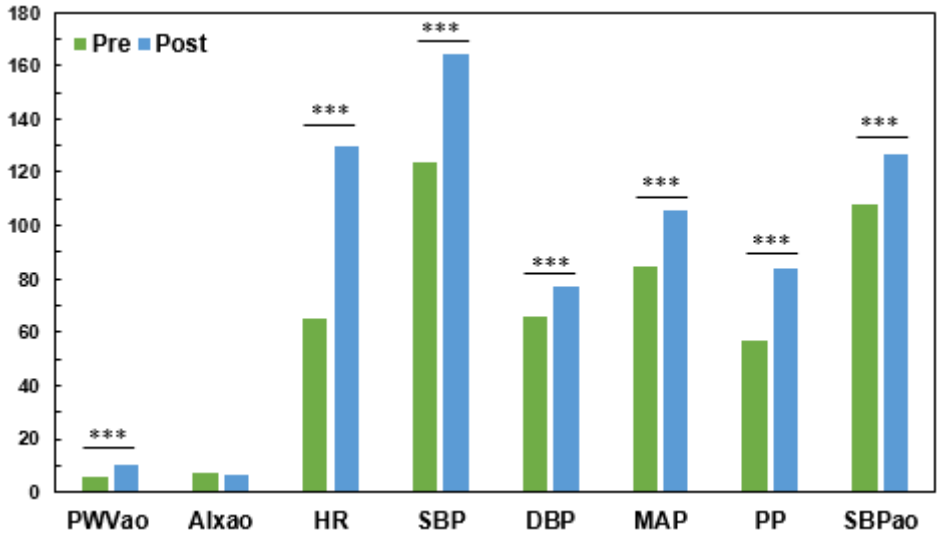

Figure 11: Illustration of the proportion between parameters previous (green) and after (blue) ergometry.
Degree of significance is illustrated as * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; aortic pulse wave velocity (PWVao), aortic augmentation index (AIxao), heart rate (HR), systolic blood pressure (Sys), diastolic blood pressure (Dia), mean arterial pressure (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao).

3.2.2. Differences in Pre Parameter Values between Groups

As described in the methods section, all participants where split up in the age-groups U10, U12, U14, U16 and U18 according to the normal squad teams of this soccer club.

The following parameters showed Pre values differences between groups: PWVao, AIxao, HR, SBP, DBP, MAP, PP and SBPao.

Differences in PWVao were found between the U18 and three youngest groups U10 (p=0.003), U12 (p=0.000), U14 (p=0.022) as well as between the U12 and the U16 (p=0.040) (Figure 13, Table 14).

Differences in AIxao were only found between the U12 and the U16 (p=0.041), U18 (p=0.000), respectively (Figure 14, Table 14).

In HR, differences were found between the oldest group U18 and the three youngest groups U10 (p=0.000), U12 (p=0.002) and U14 (p=0.000), respectively. Moreover the U16 and the youngest group (U10) showed differences (p=0.019).

SBP, as well as MAP showed differences between the two youngest groups, respectively, and the three oldest groups, respectively. SBP: U10:U14 (p=0.018), U10:16 (p=0.002), U10:U18 (p=0.023); U12:U14 (p=0.000), U12:U16 (p=0.000),

U12:18 (p=0.000). MAP: U10:U14 (p=0.001), U10:16 (p=0.002), U10:U18 (p=0.006); U12:U14 (p=0.000), U12:U16 (p=0.000), U12:18 (p=0.000).

In DBP values, differences were found between the U10 and the U14 (p=0.003), U16 (p=0.030) and the U18 (p=0.027). Additionally, the U12 differed to the U14 (p=0.003).

PP and SBPao showed differences between the U12 and the U14 (p=0.037; p=0.001), U16 (p=0.000; p=0.000) and U18 (p=0.008; p=0.032), respectively. Moreover, SBPao also showed differences between U10 and U16 (p=0.034).

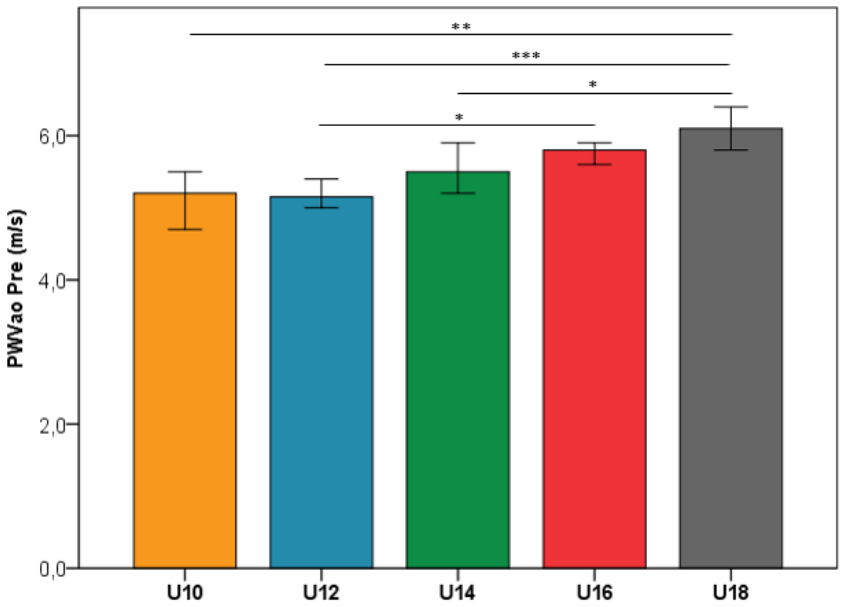

Figure 12: Illustration of Pre PWVao values in the different groups.
Note: Data expressed as median with a confidence interval (CI) of 95%.
Degree of significance is illustrated as * p < 0.05, ** p < 0.01, *** p < 0.001.

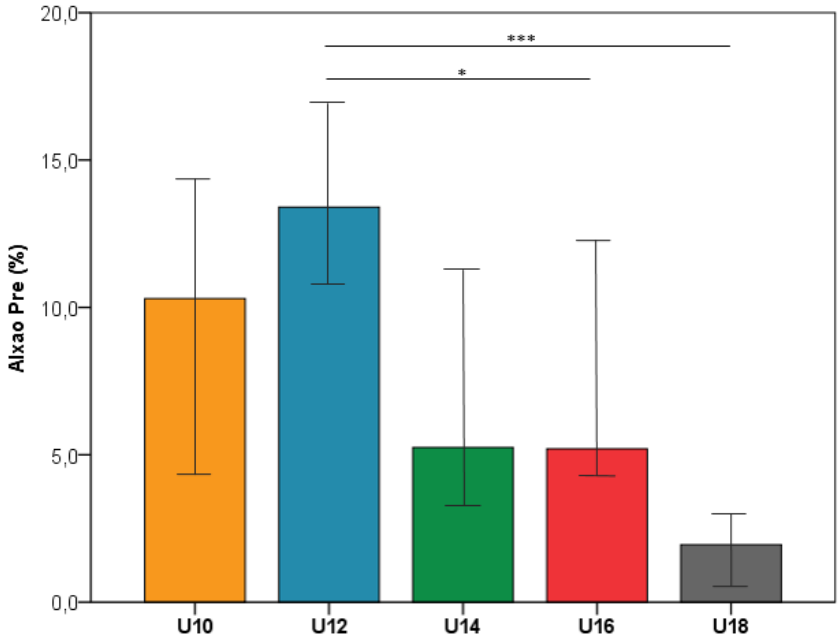

Figure 13: Illustration of Pre AIxao values in the different groups.
Note: Data expressed as median with a confidence interval (CI) of 95%.
Degree of significance is illustrated as * p < 0.05, ** p < 0.01, *** p < 0.001.

Table 14: Pre parameter values of PWVao and AIxao in the different groups and over all groups.

Group	Parameter			
	PWVao Pre	**n**	**AIxao Pre**	**n**
U10	5.3 (4.4 - 5.7)	13	10.30 (2.4 - 24.4)	13
U12	5.3 (4.5 - 6.5)	36	13.40 (4.8 - 27.9)	36
U14	5.7 (4.7 - 8.0)	39	5.25 (-3.4 - 35.2)	39
U16	5.9 (4.9 - 10.7)	47	5.20 (-4.2 - 35.7)	47
U18	6.2 (4.9 - 18.0)	37	1.95 (-3.2 - 44.1)	37
Total	5.6 (4.4 - 18.0)	172	7.20 (-4.2 - 44.1)	172

Pulse wave velocity aortic (PWVao) in m/s, augmentation index aortic (AIx) in %.
Note: Data expressed as median (minimum - maximum).

Table 15: Differences and p-values of different Pre parameters between the groups.

Parameter Pre	p-value	U10	U12	U14	U16	U18
HR	p=0.000	73 ± 9.6	69 ± 10.6	70 ± 10.7	64 ± 9.4	60 ± 7.5
Differences					U10 (p=0.019)	U10 (p=0.000) U12 (p=0.002) U14 (p=0.000)
SBP	p=0.000	117 (100 - 129)	113 (97 - 149)	125 (111 - 189)	127 (109 - 185)	127 (108 - 146)
Differences		U14 (p=0.018) U16 (p=0.002) U18 (p=0.023)	U14 (p=0.000) U16 (p=0.000) U18 (p=0.000)			
DBP	p=0.000	60 (51 - 70)	60 (47 - 81)	69 (55 - 91)	67 (50 - 97)	68 (46 - 83)
Differences		U14 (p=0.003) U16 (p=0.030) U18 (p=0.027)	U14 (p=0.003)			
MAP	p=0.000	75 (69 - 90)	78 (67 - 104)	87 (74 - 108)	86 (70 - 126)	86 (67 - 102)
Differences		U14 (p=0.001) U16 (p=0.002) U18 (p=0.006)	U14 (p=0.000) U16 (p=0.000) U18 (p=0.000)			
PP	p=0.000	57 (41 - 69)	51 (40 - 73)	56 (41 - 121)	62 (45 - 88)	58 (44 - 81)
Differences			U14 (p=0.037) U16 (p=0.000) U18 (p=0.008)			
SBPao	p=0.000	99 (91 - 114)	101 (84 - 130)	110 (94 - 192)	111 (92 - 162)	110 (93 - 141)
Differences		U16 (p=0.034)	U14 (p=0.001) U16 (p=0.000) U18 (p=0.032)			

Heat rate (HR) in beats/minute, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressures (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Date expressed in median (minimum - maximum) or for HR in mean value ± standard deviation (SD). "p-value" indicates whether or not significant differences between groups exist. If so, level of significance and between which groups, can be found underneath the corresponding group ("U10", "U12", U14", "U16", "U18").

3.2.3. Differences in Post Parameter Values between Groups

In Post values differences in PWVao were found between the two youngest groups U10 and U12, respectively to the three oldest groups U14, U16, U18, respectively. Differences between the U10 and the oldest three groups were as follows: U14 (p=0.003), U16 (p=0.000), U18 (p=0.000). Differences between the U12 to the oldest three groups were as follows: U14 (p=0.010), U16 (p=0.000), U18 (p=0.000) (Figure 15, Table 16).

In HR, differences between the U10 and all other groups were found: U12 (p=0.013), U14 (p=0.000), U16 (p=0.000), U18 (p=0.000). Differences were found between the U12 and the U14 (p=0.001), U18 (p=0.019), respectively, too.

In SBPao, difference were found between the groups U16 and U10 (p=0.023), U12 (p=0.004), U14 (p=0.002), respectively.

DBP and MAP value differences were found between the groups U10 and U12 (p=0.015; p=0.018), U14 (p=0.000; p=0.000), U16 (p=0.003; p=0.000) and U18 (p=0.030; p=0.000), respectively. Moreover in MAP differences were also found between U12 and U16 (p=0.041).

In Post systolic blood pressure values, differences were found between the two youngest groups, respectively and the three oldest groups, respectively. Differences between the U10 and the oldest three groups were as follows: U14 (p=0.000), U16 (p=0.000), U18 (p=0.000). Differences between the U12 to the oldest three groups were as follows: U14 (p=0.027), U16 (p=0.000), U18 (p=0.000). Furthermore, differences were also found between the U14 and U16 (p=0.038), U18 (p=0.022), respectively.

In PP, the three youngest groups differed from the two oldest groups, respectively. Differences were for the U18: U10 (p=0.000), U12 (p=0.000), U14 (p=0.000), and for the U16: U10 (p=0.000), U12 (p=0.000), U14 (p=0.000).

No differences in Post values between groups were found in AIxao (Figure 16, Table 16).

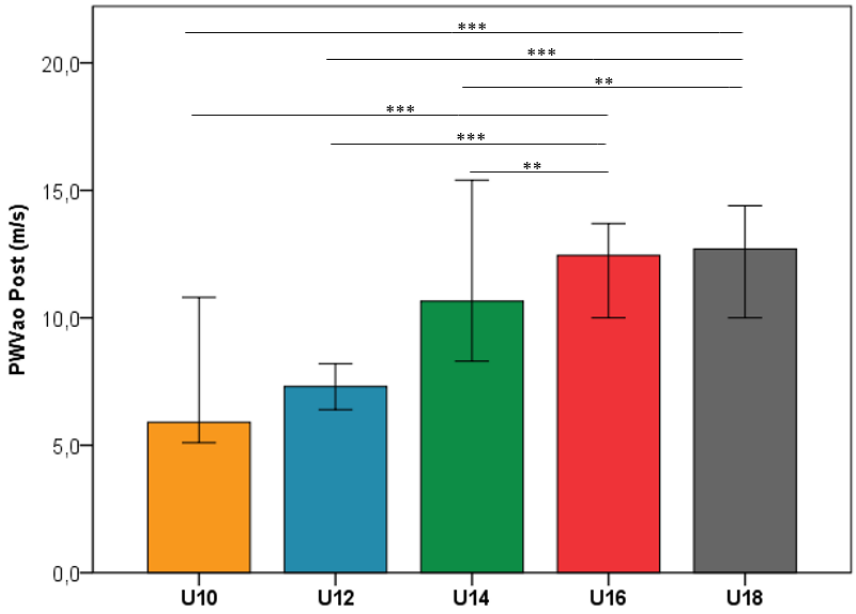

Figure 14: Illustration of Post PWVao values in the different groups.
Note: Data expressed as median with a confidence interval (CI) of 95%.
Degree of significance is illustrated as * p < 0.05, ** p < 0.01, *** p < 0.001.

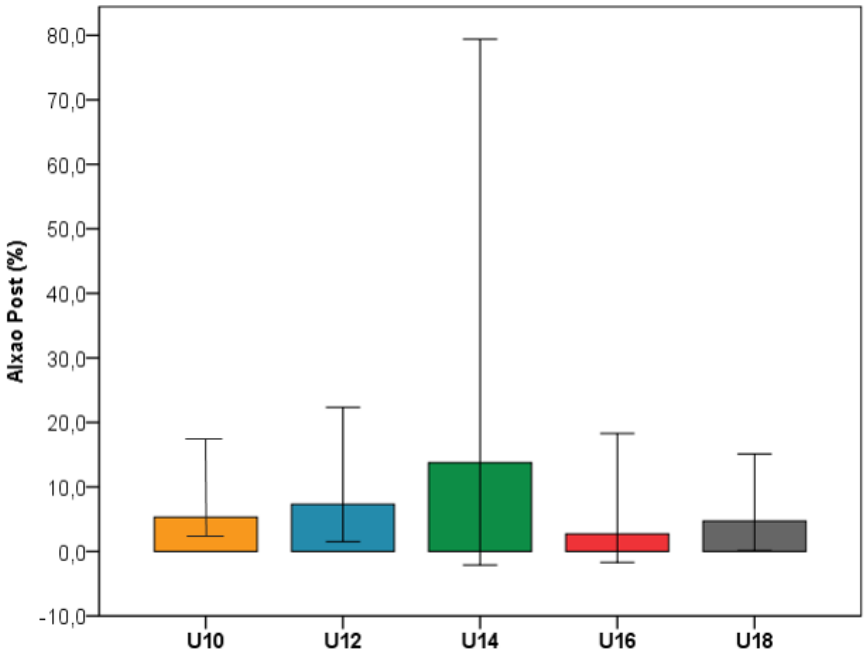

Figure 15: Illustration of Post AIxao values in the different groups.
Note: Data expressed as median with a confidence interval (CI) of 95%.
Degree of significance is illustrated as * p < 0.05, ** p < 0.01, *** p < 0.001.

Table 16: Post parameter values of PWVao and AIxao in the different groups and over all groups.

Group	Parameter			
	PWVao Post	**n**	**AIxao Post**	**n**
U10	5.9 (5.0 - 14.2)	14	5.30 (-1.3 - 32.5)	13
U12	7.3 (5.1 - 13.8)	26	7.30 (-12.3 - 84.8)	26
U14	10.7 (6.0 - 18.5)	18	13.75 (-10.8 - 85.3)	18
U16	12.4 (6.2 - 19.3)	32	2.70 (-6.0 - 84.3)	31
U18	12.8 (7.4 - 18.7)	26	4.70 (-5.8 - 83.9)	24
Total	10.3 (5.0 - 19.3)	116	6.20 (-12.3 - 85.3)	112

Pulse wave velocity aortic (PWVao) in m/s, augmentation index aortic (AIx) in %.
Note: Data expressed as median (minimum - maximum).

Table 17: Differences and p-values of different Pre parameters between the groups.

Parameter Post	p-value	U10	U12	U14	U16	U18
HR	p=0.000	99 ± 21.4	121 ± 22.8	139 ± 16.5	132 ± 18.2	135 ± 15.9
Differences		U12 (p=0.013) U14 (p=0.000) U16 (p=0.000) U18 (p=0.000)	U14 (p=0.001) U18 (p=0.019)			
SBP	p=0.000	138 (115 - 156)	152 (124 - 194)	164 (127 - 207)	173 (142 - 233)	173 (145 - 209)
Differences		U14 (p=0.000) U16 (p=0.000) U18 (p=0.000)	U14 (p=0.027) U16 (p=0.000) U18 (p=0.000)	U16 (p=0.038) U18 (p=0.022)		
DBP	p=0.000	68 (53 - 75)	78 (55 - 111)	85 (61 - 103)	79 (58 - 133)	77 (59 - 106)
Differences		U12 (p=0.015) U14 (p=0.000) U16 (p=0.003) U18 (p=0.030)				
MAP	p=0.000	90 (76 - 102)	103 (79 - 139)	107 (89 - 138)	110 (87 - 166)	108 (88 - 139)
Differences		U12 (p=0.018) U14 (p=0.000) U16 (p=0.000) U18 (p=0.000)	U16 (p=0.041)			
PP	p=0.000	72 (56 - 86)	73 (51 - 91)	80 (44 - 104)	95 (71 - 115)	97 (72 - 134)
Differences					U10 (p=0.000) U12 (p=0.000) U14 (p=0.000)	U10 (p=0.000) U12 (p=0.000) U14 (p=0.000)
SBPao	p=0.000	113 (98 - 155)	122 (92 - 165)	114 (94 - 175)	139 (104 - 206)	136 (99 - 170)
Differences					U10 (p=0.023) U12 (p=0.004) U14 (p=0.002)	

Heat rate (HR) in beats/minute, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressures (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Date expressed in median (minimum - maximum) or for HR in mean value ± standard deviation (SD). "p-value" indicates whether or not significant differences between groups exist. If so, level of significance and between which groups, can be found underneath the corresponding group("U10", "U12", U14", "U16", "U18").

3.2.4. Differences of Changes in Parameter Values due to the Intervention between the Groups

Differences between groups in value changes due to the ergometry intervention were analysed for the two arterial stiffness corresponding parameters pulse wave velocity and augmentation index.

3.2.4.1. PWVao

In PWVao significant differences between Pre and Post values were found in each age-group analysed by Wilcoxon-test. Values in the U10 increased from 5.3 to 5.9m/s (p=0.003), in the U12 from 5.3 to 7.3m/s (p=0.000), in the U14 from 5.7 to 10.7m/s (p=0.000), in the U16 from 5.9 to 12.4m/s (p=0.000) and in the U18 from 6.2 to 12.8m/s (p=0.000).

To proof significant differences in changes compared to age-groups ANOVA with repeated measures was performed and showed significant differences in effect of time (p=0.000), interaction effect (p=0.001) and group-effect (p=0.000). Therefore Post-hoc analysis with correction for Bonferroni was done.

Concerning effect of time, mean values of PWVao of all groups showed elevations after intervention (Figure 17).

Post-hoc analysis of the interaction effect showed the following differences between groups: The two youngest groups (U10 and U12), each, showed differences to the three oldest groups (U14, U16, U18), respectively. Differences to these groups for the U10 were: p=0.002 (U14), p=0.000 (U16) and p=0.000 (U18). For the U12 following differences were found: p=0.005 (U14), p=0.000 (U16) and p=0.000 (U18).

Post-hoc analysis of the group-effect revealed differences in PWVao between the two youngest groups, U10 and U12, respectively and the three oldest groups, U14, U16 and U18, respectively. Differences for the U10 to these groups were: p=0.002 (U14), p=0.000 (U16), p=0.000 (U18) and for the U12 to these groups were: p=0.005 (U14), p=0.000 (U16) and p=0.000 (U18).

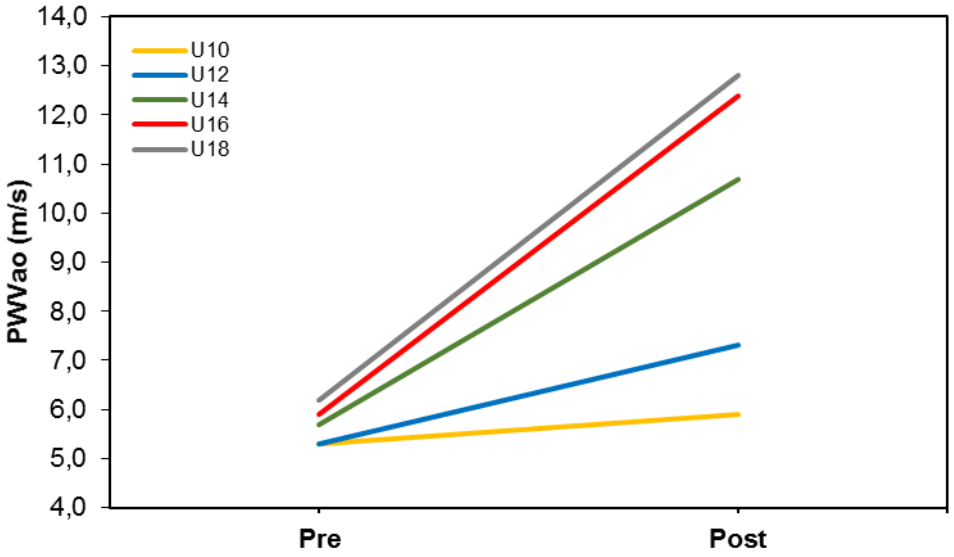

Figure 16: Representation of the changes in PWVao between the Pre and Post measurement in the different groups.
Note: Data illustrated as medians.

3.2.4.2. AIxao

ANOVA with repeated measures showed significant differences only in effect of time (p=0.001), but not in interaction effect (p=0.185) nor in group-effect (p=0.457).

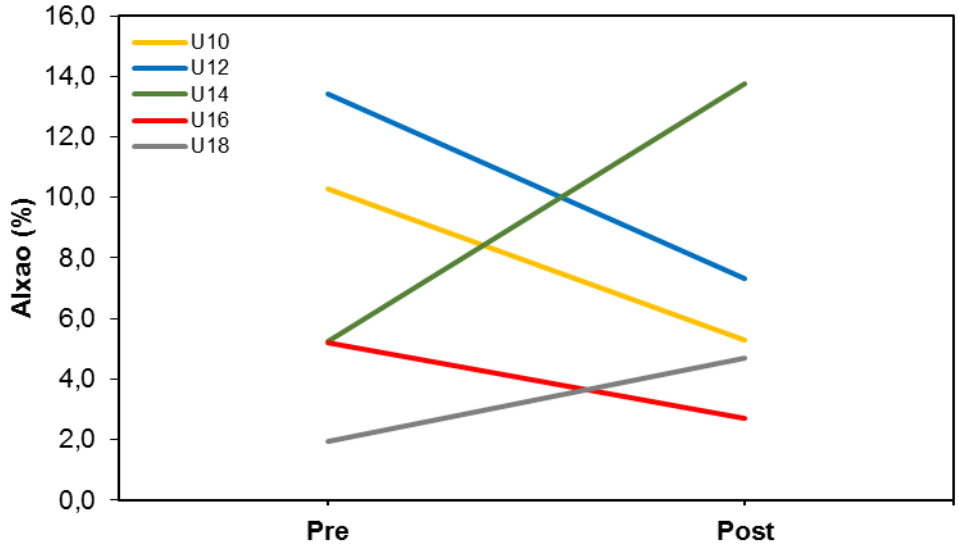

Figure 17: Representation of the changes in AIxao between the Pre and Post measurement in the different groups.
Note: Data illustrated as medians.

3.2.4.3. ∆PWVao

ANOVA analysis indicated differences between the groups (p=0.001). Post-hoc analysis with Bonferroni correction revealed differences in ∆PWVao between the U10 and the U16 (p=0.013) as well as between the U12 and the U16 (p=0.015). Furthermore, a difference between the U10 and U18 (p=0.042) was found (Table 18).

Table 18: Representation of the ∆PWVao and ∆AIxao values for the age-groups.

Age-group	∆PWVao	∆AIxao
U10	2.2	-0.6
U12	3.0	5.4
U14	5.7	25.5
U16	5.9	8.4
U18	5.6	15.2

Pulse wave velocity aortic (PWVao) in m/s, augmentation index aortic (AIxao) in %.
Note: Data expressed as means

3.2.4.4. ∆AIxao

In contrast to ∆PWVao, no differences between the groups in ∆AIxao were found (Table 18).

3.3. Correlation Analysis

Correlations between parameters were analysed in the different groups but also over all groups and described and illustrated in this chapter.

3.3.1. Correlation Analysis over all Groups

Correlation analyses over all groups (Table 19) revealed that ∆PWV were positively associated with Watt/kg ($p<0.02$; $\rho=0.225$), Watt_absolute ($p<0.001$; $\rho=0.447$), Age ($p<0.001$; $\rho=0.391$) and Post PWVao ($p<0.001$; $\rho=0.948$). Moreover, analysis revealed positive associations between Post PWVao and Pre PWVao ($p<0.001$; $\rho=0.326$), Watt/kg ($p<0.05$; $\rho=0.201$), Age ($p<0.001$; $\rho=0.512$), Watt_absolute ($p<0.001$; $\rho=0.544$), respectively. Furthermore, Watt_absolute revealed positive correlations with Pre PWVao ($p<0.001$; $\rho=0.470$), ∆PWV ($p<0.001$; $\rho=0.447$), age ($p<0.001$; $\rho=0.914$), respectively, and negative correlations with Pre AIxao ($p<0.001$; $\rho=0.489$). Additionally, correlation analysis over all groups revealed that Age was positively associated with Pre PWVao ($p<0.001$; $\rho=0.518$) and negatively associated with Pre AIxao ($p<0.001$; $\rho=0.494$) and that ∆PWVao ($p<0.001$; $\rho=0.338$) and Pre PWVao ($p<0.001$; $\rho=0.292$) are negatively associated with Pre AIxao, respectively. Last but not least, Pre AIxao showed a negative association with Post PWVao ($p<0.001$; $\rho=0.367$).

All significant associations as well as the corresponding correlation coefficients are illustrated in the figures 18 - 32.

Table 19: Associations between arterial stiffness parameters (PWV and AIx), workload and age over all participants.

	PWVao Pre	PWVao Post	∆PWVao	AIxao Pre
Age	0.518***	0.512***	0.391***	- 0.494***
Watt absolute	0.470***	0.544***	0.447***	- 0.489***
Watt/kg	n.s.	0.201*	0.225*	n.s.
PWVao Pre	-	0.326***	n.s.	- 0.292***
∆PWVao	n.s.	0.948***	-	- 0.338***
AIxao Pre	- 0.292***	- 0.367***	- 0.338***	-

Note: Data indicate Spearman-Rho correlation coefficients. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Pulse wave velocity aortic (PWVao), augmentation index aortic (AIxao), not significant (n.s.)

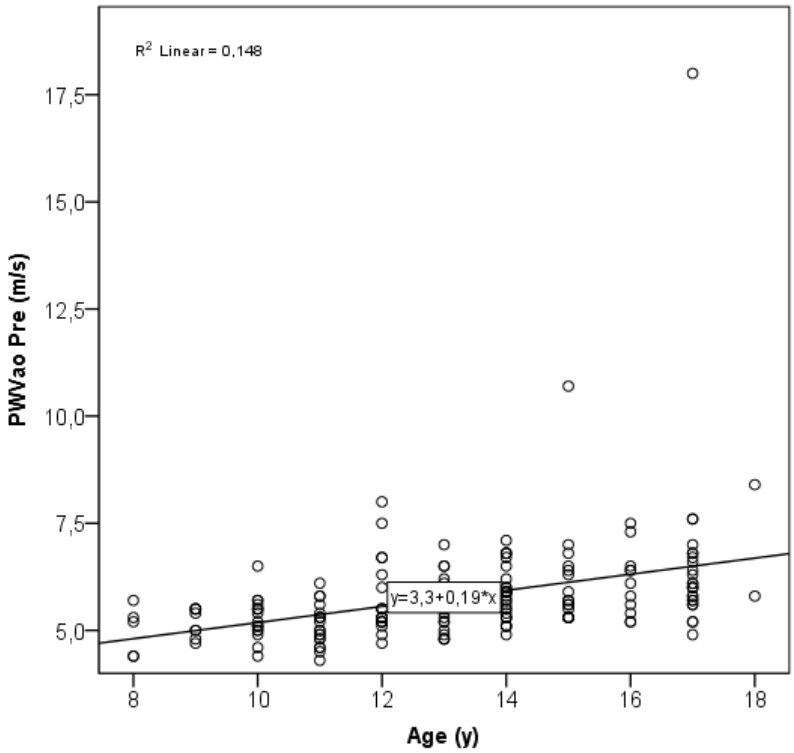

Figure 18: Illustration of the correlation between age and PWVao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

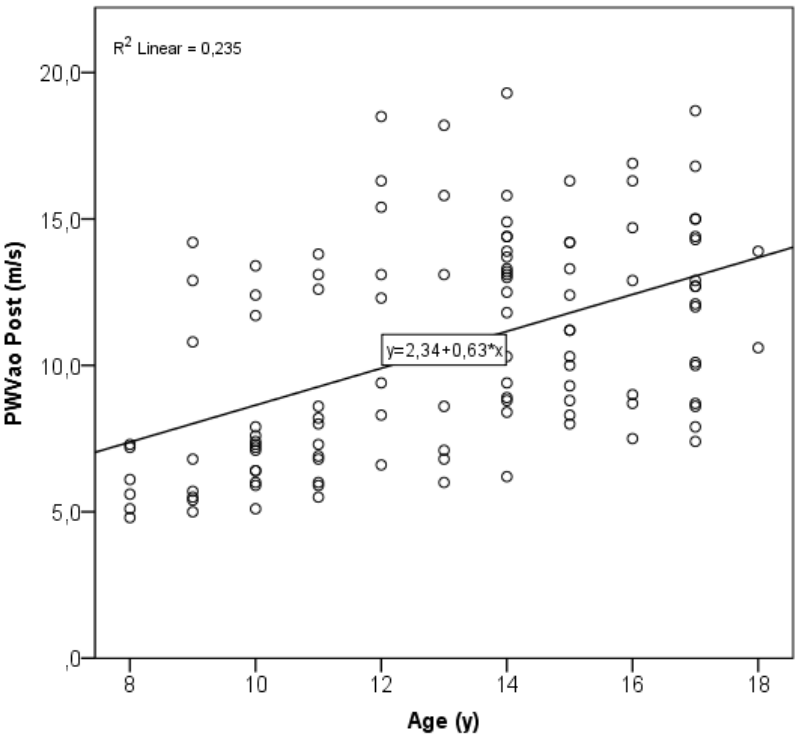

Figure 19: Illustration of the correlation between age and PWVao Post. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

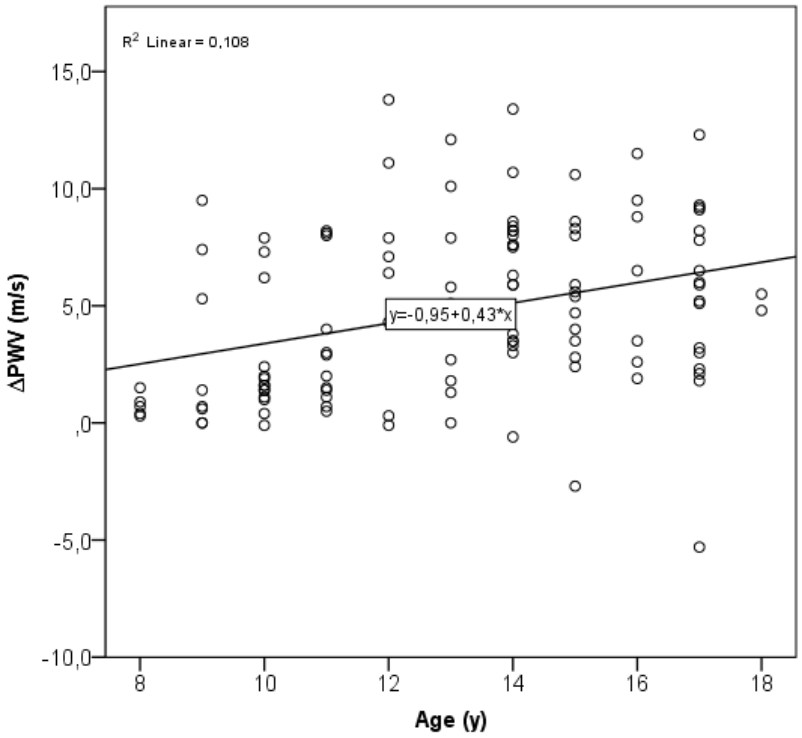

Figure 20: Illustration of the correlation between age and ∆PWV. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

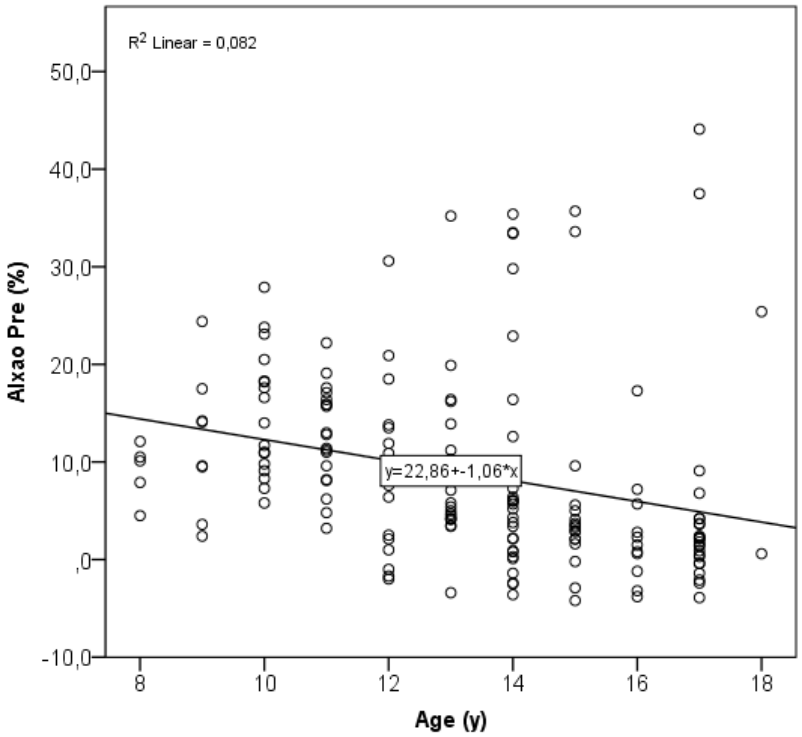

Figure 21: Illustration of the correlation between age and AIxao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

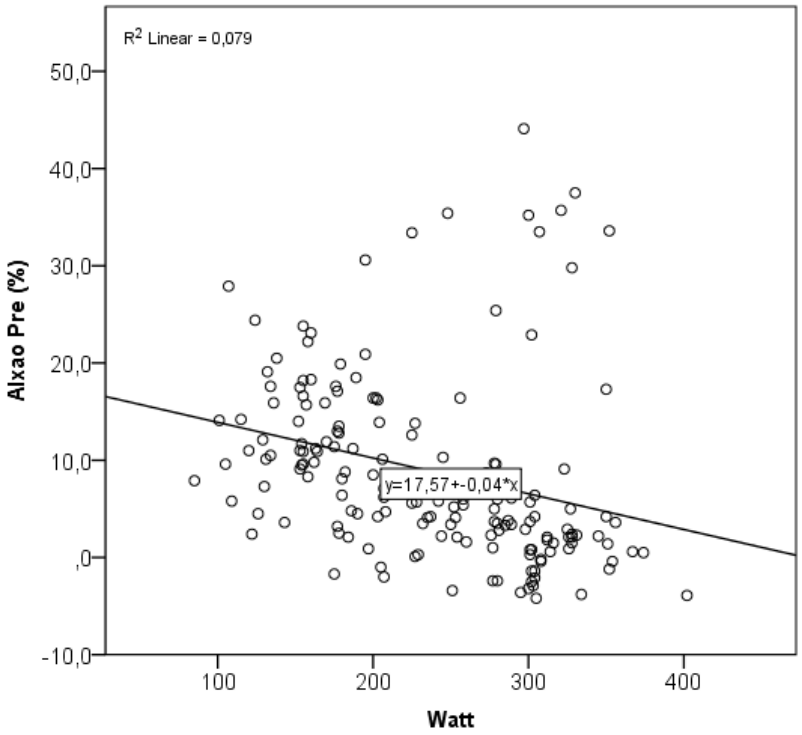

Figure 22: Illustration of the correlation between Watt and AIxao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

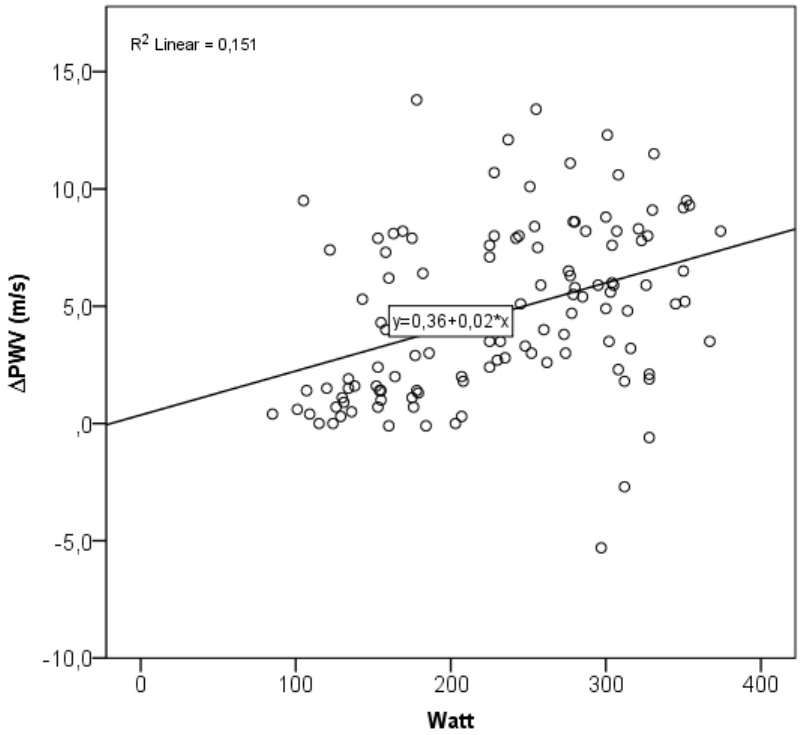

Figure 23: Illustration of the correlation between Watt and ∆PWV. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

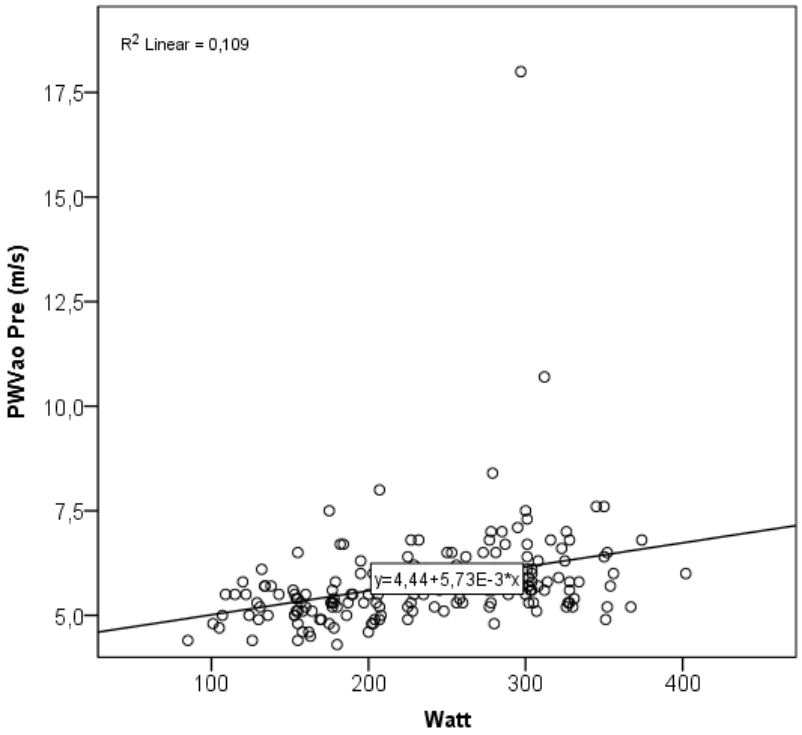

Figure 24: Illustration of the correlation between Watt and PWVao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

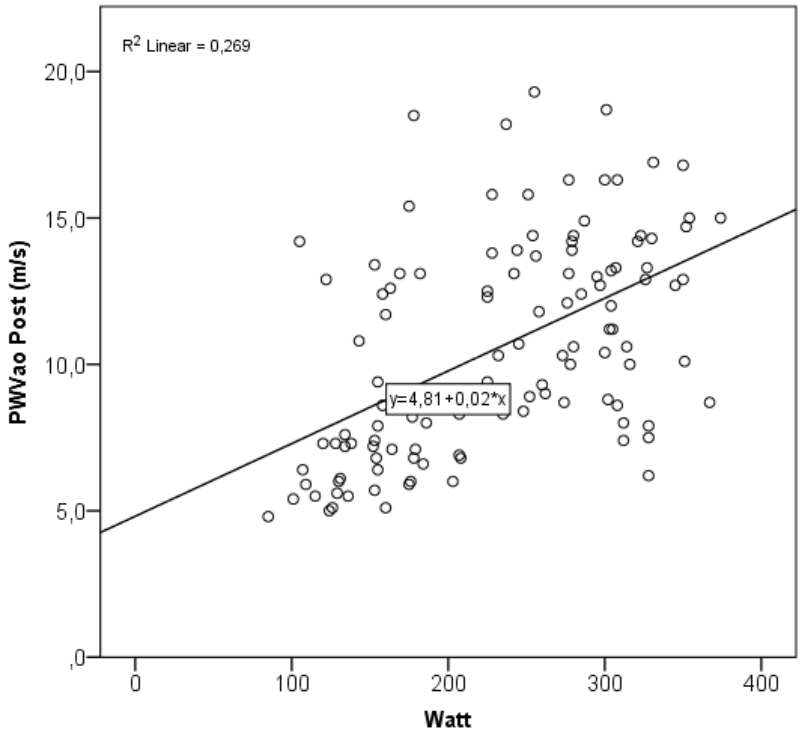

Figure 25: Illustration of the correlation between Watt and PWVao Post. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

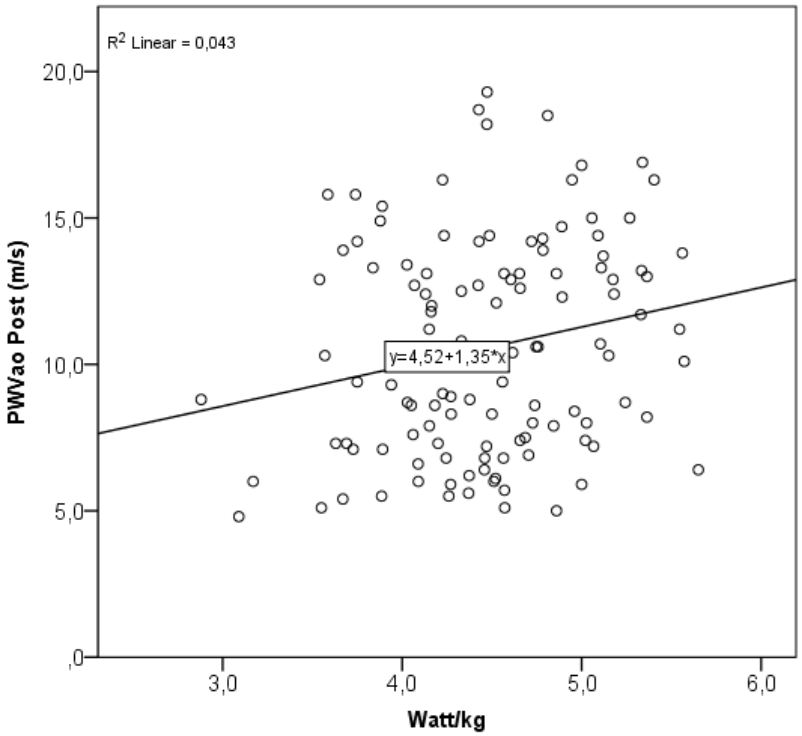

Figure 26: Illustration of the correlation between Watt/kg and PWVao Post. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

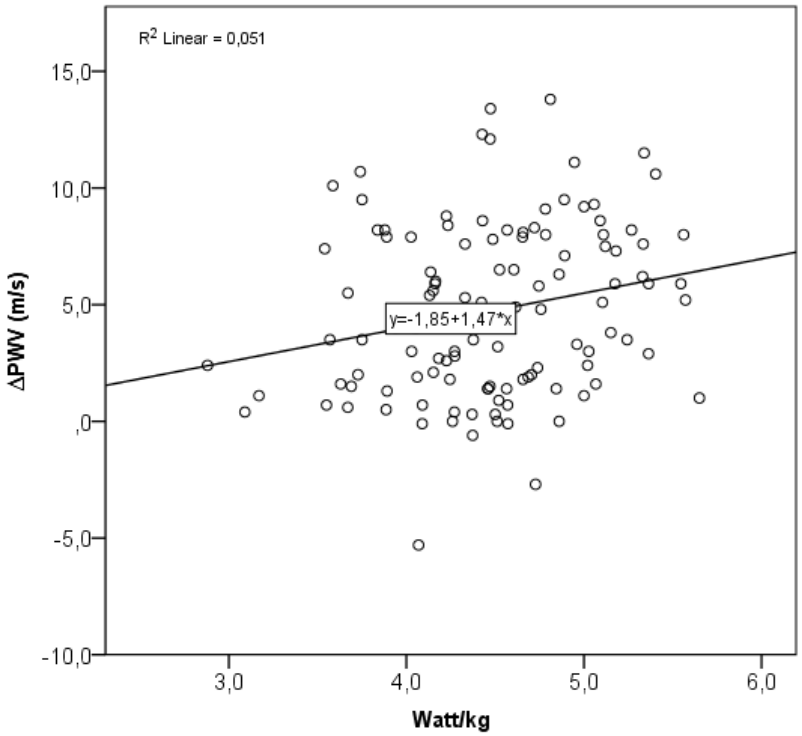

Figure 27: Illustration of the correlation between Watt/kg and ∆PWV. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

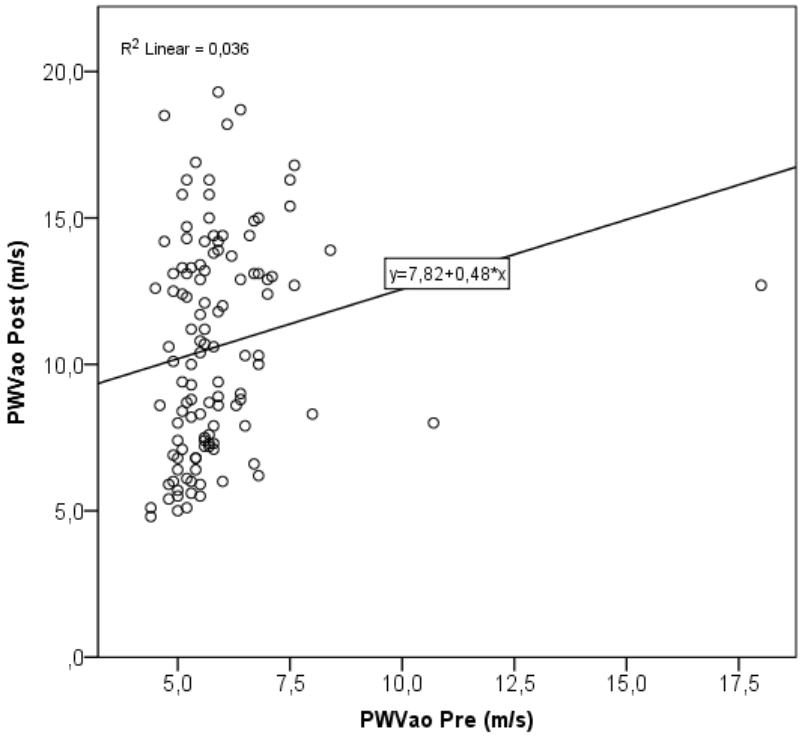

Figure 28: Illustration of the correlation between PWVao Pre and PWVao Post. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

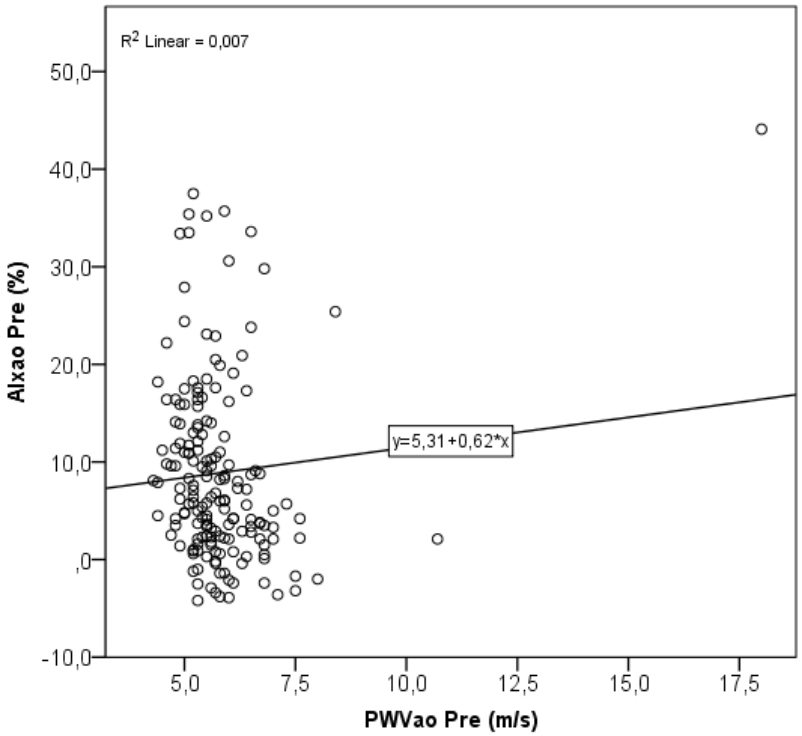

Figure 29: Illustration of the correlation between PWVao Pre and AIxao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

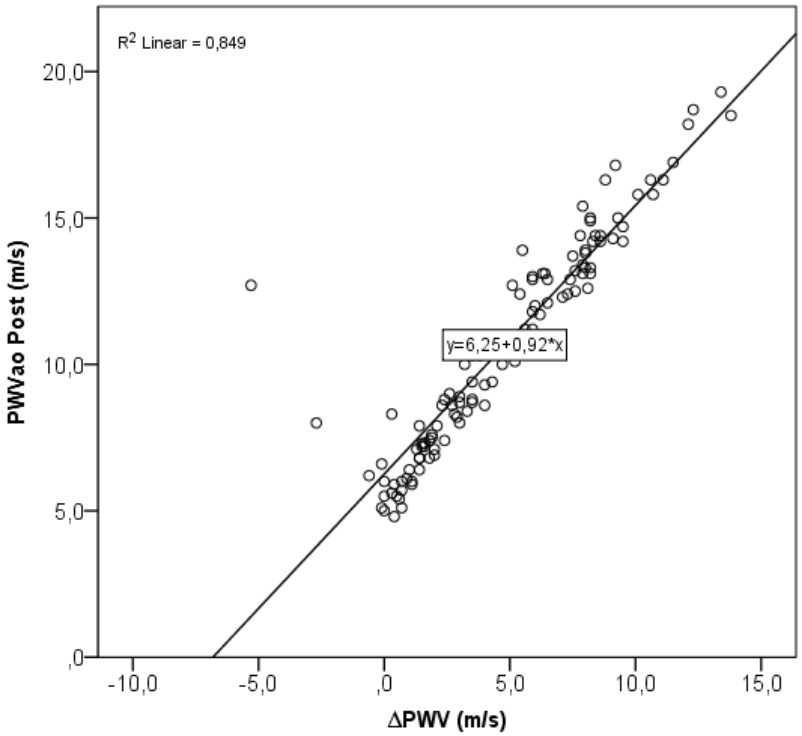

Figure 30: Illustration of the correlation between ΔPWV and PWVao Post. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

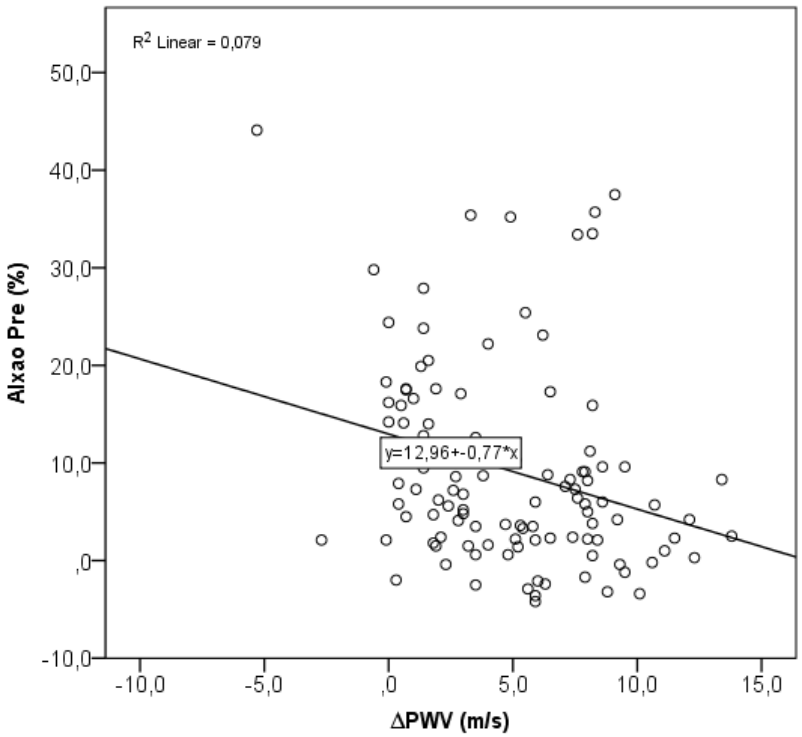

Figure 31: Illustration of the correlation between ΔPWV and AIxao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

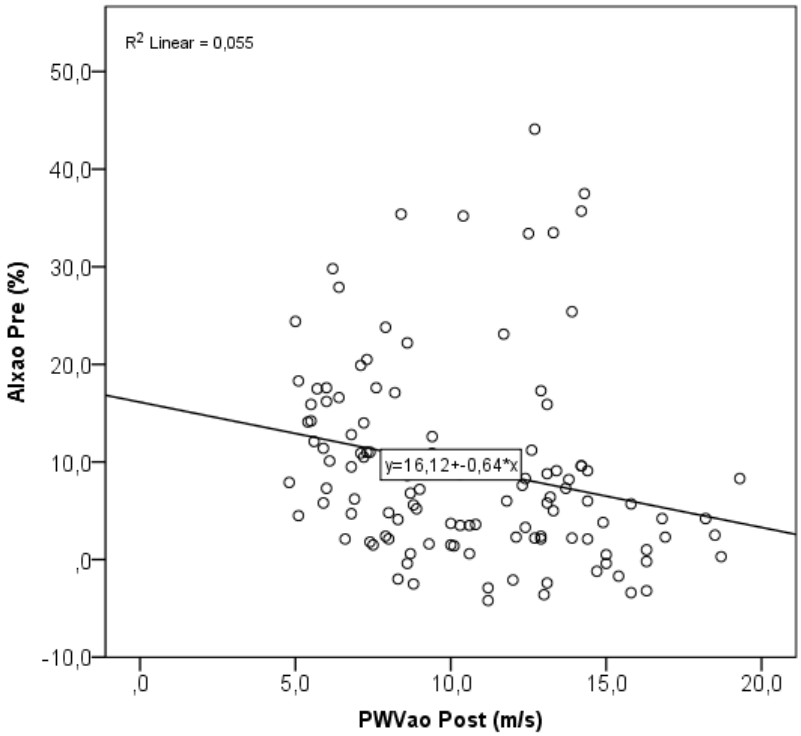

Figure 32: Illustration of the correlation between PWVao Post and AIxao Pre. The coefficient of determination (R2 Linear) indicating the degree of linear correlation between these two parameters.

3.3.2. Correlation Analysis within the Groups

When data were divided for the age-groups only one consistent correlation was found in all age-groups. As in the total collective, over all groups, a significant correlation was found between PWVao Post and ΔPWVao.

These correlatations were for the different age-groups as follows: U10: ($p<0.001$; $\rho=0.889$), U12: ($p<0.001$; $\rho=0.941$), U14: ($p<0.001$; $\rho=0.984$), U16: ($p<0.001$; $\rho=0.972$), U18: ($p<0.001$; $\rho=0.899$).

4. Discussion

In this study the participants were young, male soccer players aged 8 - 18 years. Prior to the realisation of this study, a medical preliminary assessment was performed. Within the scope of this screening an ECG was taken, body weight and body height were measured and BMI was calculated.

If the medical preliminary assessment did not show any reasons for exclusion the measurement of arterial stiffness as well as blood pressure measurements at rest were performed after which the participants performed a cycle ergometer stress testing to exhaustion. Immediately afterwards, a second, post exhaustion, arterial stiffness and blood pressure measurement was done.

A cycle ergometer stress test was chosen due to its better measurability of blood pressure and ECG in contrast to a stress test on a treadmill. Even though the participants were soccer players and therefore a treadmill ergometer test would have been more discipline specific, a better and more correct measurement of physiological data like blood pressure and ECG was more important.

A test protocol which started at 1 Watt/kg and which was increased for 25 Watt every minute was used. Especially for the younger participants a time increment of 1 minute and a total exercise time beyond 10 minutes was important in order to prevent local muscle fatigue before cardiovascular exhaustion (Hebestreit 2004). The participants were, according to their youth squads, divided into five groups, U10, U12, U14, U16 and U18.

4.1. Descriptive Statistics

4.1.1. BMI

In all age-groups, BMI values met the reference values of the “BMI-for-age in Boys, 5 to 19 years z-scores” of the World Health Organisation (WHO) (**http://www.who.int/growthref/who2007_bmi_for_age/en/** ; z-scores: boys, pdf; access on the 21.05.2014).

Table 20: BMI values of this study for the age-groups in comparison with BMI reference ranges of the WHO for the age-group equivalent age ranges in boys.

Age-group	BMI values	BMI reference values	Age range (Year: Month)
U10	16.3	15.7 - 16.4	8:0 - 9:11
U12	16.6	16.4 - 17.5	10:0 - 11:11
U14	17.8	17.5 - 18.9	12:0 - 13:11
U16	20.4	19.0 - 20.4	14:0 - 15:11
U18	22.0	20.5 - 22.2	16:0 - 18:11

Left: BMI median values collected in this study for the age-groups. Right: BMI median reference value ranges of the WHO for the age ranges corresponding to the different age-groups of the study. BMI in kg/m^2.

BMI, in median values, for the different age-groups of this study were 16.3 for the U10, 16.6 for the U12, 17.8 for the U14, 20.4 for the U16 and 22.0 for the U18. The reference value range of the WHO is 15.7 - 16.4 in the 8 - 9 years old, 16.4 - 17.5 in the 10 - 11 years old, 17.5 - 18.9 in the 12 - 13 years old, 19.0 - 20.4 in the 14 - 15 years old and 20.5 - 22.2 in the 16 - 18 years old.

The WHO defines BMI cuff-off points and BMI within all ages as normal when being within ± 1SD. Therefore the BMI values measured in the different age-groups in this study not only can be accounted just within borders for normal values but meeting exactly the median values given by the WHO.

As the individuals participating in this study were active soccer players, these, meeting the reference values of the WHO was assumed and was no surprise.

4.1.2. Heart Rate

In this study, heart rate was measured at rest (HR Pre), during the exercise testing and after the exhaustion (HR Post) in the cause of the post arterial stiffness measurement. The maximal heart rate (HR_{max}) during the exercise was obtained by means of ECG.

In general, heart rate has a wide physiological range and values of resting heart rate between 60 - 70 in untrained adults are being considered as normal (Weineck 2010). Nevertheless, in athletes and endurance trained individuals, a reduced heart rate at rest is a classic finding (Lahiri et al. 2008).
Studies have shown that with increasing size of the heart in athletes, resting heart rate but not maximal heart rate decreases (Findeisen et al. 1980).
Another reason for a decreased resting heart rate as a result of physical exercise training, especially endurance training, is the decreased activity of the sympathetic and the increased activity of the parasympathetic nervous system.
Furthermore, as children and adolescents have smaller hearts, they show, at rest as well as under physical stress, higher heart rates (Weineck 2010).

For both, HR Pre values as well as HR_{max} values of this study, similar values can be found in the literature (Goldberg et al. 1966, Alpert et al. 1982, Mahon et al. 2010).

On the other hand, for HR_{max}, there are also studies which state more or less different values like, Ten Harkel et al. (2011) who found HR_{peak} values in the cause of a cycle ergometer exercise testing which were below ours with 184 ± 12 beats/minute. Also, Aandstad et al. (2006) investigated HR_{max} in 9 and 10 year old Norwegian schoolchildren and found a mean value for boys of 193.5 in contrast to subjects of that age-group in our study with mean values of 187 (U10) and 190 (U12). Thus, values of our study lying slightly beyond the ones of the Norwegian subjects but above the ones of the study by Ten Harkel et al. (2011). In 8 - 11 year old boys, in a study by Dencker et al. (2007), HR_{max} values very similar to ours (188 beats per minute) were found.
These different values of the different studies show the wide, normal, physiological range of HR_{max} and its inter-individual-dependency.
However, another reason for lower maximal heart rates, considering similar stress testings with similar protocols, could be the degree of exhaustion. Athletes could

be differently strong motivated and therefore keep on cycling and exhausting themselves to a higher degree than others. In fact, motivation is always a parameter that has to be taken into account.

HR Post measurements took place approximately 3 minutes after the ergometry was finished. While HR Pre values decreased with increasing age (-groups), Post values increased. As a result the, differences between Pre and Post values also increased with increasing age (-groups). This indicates that the cycle ergometer stress testing had higher influences on the older groups than on the younger groups. However, HR_{max} values did not show that different values indicating a similar exhaustion in the different groups.
The Post values of all groups were beyond the HR_{max} values of this study and on average were 67% of the HR_{max} indicating a recovery after the exhaustion. Between the groups, the HR Post values, expressed as percentage of the HR_{max}, demonstrated only little differences. Only the two youngest groups and especially the U10 showed lower values than the older groups. This could be the result of the older groups recovering more slowly from the exhaustion or of the younger groups having themselves not exhausted as much as the older groups have.

4.1.3. Blood Pressures

Considering the blood pressure reference values at rest of the “Deutsche Hochdruckliga” for children and adolescents, 68.4% of the 8 - 15 year old and 59.5% of the 16 - 18 year old participants of this study would have to be considered as hypertonic or high normotonic (Table 21 and 22). This means that 66.5%, almost two thirds, of the whole study population would have to be considers as at least high normotonic. This appears to be especially dramatic and even surprising as one would think of active soccer athletes as healthy and with a well-trained and well-functioning cardiovascular system and rather lower blood pressure values in contrast to non-athletes.

Table 21: Blood pressure parameters before the ergometry in the groups and over all groups.

Group	Parameter Pre				
	SBP	**DBP**	**MAP**	**PP**	**SBPao**
U10 (n=14)	117 (100 - 129)	60 (51 - 70)	75 (69 - 90)	57 (41 - 69)	99 (91 - 114)
U12 (n=36)	113 (97 - 149)	60 (47 - 81)	78 (67 - 104)	51 (40 - 73)	101 (84 - 130)
U14 (n=39)	125 (111 - 189)	69 (55 - 91)	87 (74 - 108)	56 (41 - 121)	110 (94 - 192)
U16 (n=47)	127 (109 - 185)	67 (50 - 97)	86 (70 - 126)	62 (45 - 88)	111 (92 - 162)
U18 (n=37)	127 (108 - 146)	68 (46 - 83)	86 (67 - 102)	58 (44 - 81)	110 (93 - 141)
Total (n=173)	124 (97 - 189)	66 (46 - 97)	85 (67 - 126)	57 (40 - 121)	108 (84 - 192)

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP), systolic aortic blood pressure (SBPao) in mm Hg.
Note: Data expressed as median (minimum - maximum).

However, in children and adolescents it is not that simple. In contrast to adults, where certain widely accepted reference and threshold values for blood pressures and hypertension exist, in children and adolescents this is not the case. For these, what is to be considered a normal blood pressure depends on several factors like height, age and sex, with the most relevant being height. The fact that children and adolescents do not all grow the same and at the same time, makes it complicate and even senseless to express universal thresholds for children of all ages and body stature. Shorter children and adolescents will have lower normal blood pressures as taller ones. Therefore, it is totally normal for children and adolescents to get higher blood pressures when growing taller (Falkner & Daniels 2004).

Table 22: Reference and threshold values for blood pressure in children and adolescents. (Deutsche Hochdruckliga – Deutsche Gesellschaft für Hypertonie und Prävention, http://www.hochdruckliga.de/blutdruckwerte-von-kindern.html, access on the 21.05.2014).

Age	Blood Pressure	normal	high normal	hypertension
12	systolic	< 120	120 - 125	> 125
	diastolic	< 75	75 - 80	> 80
16	systolic	< 125	125 - 135	> 135
	diastolic	< 80	80 - 85	> 85
> 18	systolic	< 130	130 - 140	> 140
	diastolic	< 85	58 - 90	> 90

Note: Age in years, blood pressure in mm Hg.

As a result, in children and adolescents, normal blood pressure is defined as being <90th percentile for sex, age and height. Blood pressure values ≥90th percentile but <95th percentile are defined as “prehypertension” or “high normal” and values ≥95th percentile are defined hypertension. That goes for systolic blood pressure as well as diastolic blood pressure. Furthermore, in adolescents, blood pressure is defined as “prehypertension” when <95th percentile and ≥ 120/80mm Hg regardless whether this is ≥90th percentile or not (Falkner & Daniels 2004).

Table 23 shows the percentiles for systolic and diastolic blood pressure in this investigation according to the age and age-groups, respectively. Due to a small “n”, 90th and 95th percentile, mentioned above as important in order to define blood pressure threshold values, could not be estimated. In comparison with percentile reference values (see Appendix) by Rosner et al. (2008) and Neuhauser et al. (2011), still the blood pressures of the participants of this study are surprisingly high.

Table 23: Representation of the percentile limits for systolic and diastolic blood pressure of the participants of this investigation by age and age-groups.

Age-group	Age		Percentiles						
			5%	**10%**	**25%**	**50%**	**75%**	**90%**	**95%**
U10 (n=14)	8 (n=6)	Systolic	102	102	108	114	121	**-**	**-**
		Diastolic	51	51	51	57	62	**-**	**-**
	9 (n=8)	Systolic	100	100	106	116	128	**-**	**-**
		Diastolic	54	54	55	61	64	**-**	**-**
U12 (n=36)	10 (n=17)	Systolic	97	99	106	110	118	**124**	**-**
		Diastolic	47	53	58	60	65	**72**	**-**
	11 (n=19)	Systolic	101	101	106	113	120	**142**	**-**
		Diastolic	50	51	54	59	67	**79**	**-**
U14 (n=39)	12 (n=18)	Systolic	111	114	118	122	130	**136**	**-**
		Diastolic	57	60	62	66	70	**72**	**-**
	13 (n=21)	Systolic	111	113	123	126	137	**146**	**185**
		Diastolic	55	56	65	70	75	**78**	**90**
U16 (n=47)	14 (n=30)	Systolic	110	116	120	126	137	**143**	**168**
		Diastolic	51	52	62	68	72	**78**	**87**
	15 (n=17)	Systolic	114	116	124	128	131	**139**	**-**
		Diastolic	55	55	60	62	71	**79**	**-**
U18 (n=37)	16 (n=11)	Systolic	112	113	118	124	132	**144**	**-**
		Diastolic	53	54	60	66	73	**76**	**-**
	17 (n=24)	Systolic	109	112	118	130	137	**141**	**145**
		Diastolic	48	54	60	68	73	**76**	**81**
	18 (n=2)	Systolic	114	114	114	121	-	**-**	**-**
		Diastolic	64	64	64	72	-	**-**	**-**

Note: Due to the little "n" in certain ages, no 90^{th}, 95^{th} or 75^{th} percentile could be estimated. Age in years, percentiles of blood pressure values in mm Hg.

Nevertheless, the second criteria in order to define the blood pressure of an individual as hypertonic is that it has to be so on three or more separate occasions (Falkner & Daniels 2004, "Deutsche Hochdruckliga – Deutsche Gesellschaft für Hypertonie und Prävention" (http://www.hochdruckliga.de/blutdruckwerte-von-kindern.html, access on the 21.05.2014)).

In conclusion, in order to determine whether a child or adolescent is, regarding its blood pressure, normotonic, high normal or hypertonic, the subjects has to be measured at least at three different occasions with values above a certain threshold specific for its sex, height and/or age. Therefore, no further analysis

regarding the blood pressure state at rest of the participants of this study is being made, due to the fact that only one measurement at rest was done.
Nevertheless, two different lists of percentiles for blood pressure comparison can be found in the section “Appendix” of this study.

Blood pressure during the cycle stress test to exhaustion as well as maximal blood pressure were within the physiological range. No further abnormalities were discovered. An exaggerated increase in blood pressure with a systolic pressure of more than 240mm Hg and/or a diastolic blood pressure of more than 120mm Hg as well as a progressively decrease in systolic blood pressure would have led, according to recommendations by Bar-Or (1986, p. 418), to a stop of the ergometry.

Mean brachial PP at rest over all groups of our study was 57mm Hg with significant differences between the U12 and the U14, U16 and the U18, respectively. Even though the mean values of all groups were above the ones estimated in non-obese children by Chandramohan et al. (2012), they were still within the threshold values postulated by several other studies. Wojciechowska et al. (2006) for example suggested 60mm Hg for peripheral PP and 40mm Hg for central PP as threshold values. In another study, by Asmar et al. (2001), similar threshold values, 65mm Hg, were postulated. As in further studies (Benetos et al. 1997b, Pedrinelli et al. 2000) likewise PP values were associated with cardiovascular morbidity and mortality, the thresholds of Wojciechowska et al. (2006) and Asmar et al. (2001) seem plausible.
Furthermore, the PP value data presented by Chandramohan et al. (2012) included boy and girls and even though there is no difference in gender expected in the younger participants before puberty, there might be different values in the post-puberty participants when selected for sex.

An increased systolic blood pressure is known to be correlated with higher risk of cardiovascular events. Likewise, in PP, Klassen et al. (2002) demonstrated, that with every 10mm Hg increase a 12% increase in hazard of death was associated.

Nevertheless, as the PP values gained in this study where beyond the threshold reference values of several investigations, these can be considered as normal, representing healthy PP conditions in the soccer athletes.

Post exercise PP values of our study were increased in comparison to Pre values with an average over all groups of 84mm Hg. We could not find reference values for PP after a physical stress testing to exhaustion but as during physical load, systolic blood pressure increases to a higher extend than diastolic blood pressure, the difference between these, hence PP, becomes larger than at rest.
In PP Post values, significant differences were found between the three youngest groups and the two oldest groups, respectively, with the older groups having the higher PP values. This indicates that the difference between systolic and diastolic blood pressure was higher in these two groups. As mentioned before, diastolic blood pressure increases less than systolic blood pressure and even tends to stay constant, which indicates that the systolic blood pressure rather than the diastolic blood pressure is the one responsible for the higher PP in the U16 and the U18.
As systolic blood pressure in younger children, in general, is lower than in older children and adolescents (Bar-Or 1986, p. 35) a higher PP in the older groups is a consequence of biological age. In fact, blood pressure is dependent of the body height and the younger groups showed lower mean body height than the older groups, resulting in lower normal systolic blood pressure (Falkner & Daniels 2004) and therefore in lower PP.

Evidence has demonstrated that, central systolic blood pressure shows smaller values than peripheral systolic blood pressure (Wilkinson et al. 2000, Weber et al. 2008, Schillaci & Grassi 2010). Differences between peripheral and central systolic blood pressure between 1 to 33mm Hg can be found (Nakamura et al. 2005).
In our study, both, central, aortic systolic blood pressure in Pre as well as in Post values was beyond the peripheral systolic blood pressure values. On average, over all groups at rest, peripheral systolic blood pressure was 16mm Hg higher than central systolic blood pressure indicating a normal relationship between these two systolic pressures as a difference between central and peripheral systolic blood pressure of up to 20mm Hg is considered as normal (Wilkinson et al. 2000).

After the ergometry to exhaustion, the difference between peripherally and centrally measured systolic blood pressure was larger with an average difference over all groups of 37mm Hg, mainly because peripheral systolic blood pressure demonstrated a proportionally higher increase than central systolic pressure. At rest, higher peripheral, in contrast to central, blood pressure values are due to the spatial proximity of peripheral arteries and wave reflections and an increase in arterial stiffness towards the periphery (Weber et al. 2008, Avolio et al. 2009,

Schillaci & Grassi 2010). During and after a physical load and exhaustion this relationship stays the same, hence resulting in higher central than peripheral systolic blood pressure. The reason why the difference between central and peripheral values are larger in Post values in comparison to the Pre values is that during and after exhaustion, arterial stiffness increases and therefore contributes to higher pressure amplification. Although decreasing peripheral resistance, due to dilating peripheral vessels during a physical load, peripheral systolic blood pressure still increases. This is because the increase in cardiac output during a physical load usually is more pronounced than the decrease in peripheral resistance (Alpert & Fox 1993), thus resulting in a net increase of peripheral systolic pressure.
Furthermore, in children, smaller and shorter peripheral vessels could account for an even lower peripheral resistance, resulting in a lesser increase in peripheral systolic blood pressure than in adults and adolescents (Bar-Or 1986, p. 35).

4.1.4. Watt and maximal Oxygen Consumption

Achieved absolute Watts increased with increasing age-groups from minimal 127 Watt in the U10 to maximal 316 Watt in the U18 with a median of 233.5 Watts over all age-groups. In Watt/kg, achieved values were similar between all groups with the U10 having the smallest values and being the only group significantly different to all other groups except the U16. The Watt/kg ranged between 4.30 and 4.69 and apart from the values of the U10 showed almost identical values.

When compared with the literature, lower values for both, Watt absolute and Watt/kg are found, most possibly due to the fact, that the subjects in this study were soccer athletes in comparison to non-athletes in the other studies. In a yet unpublished diploma thesis by Hudececk (2014) from our working group, 11 - 13 year old boys were investigated for aerobic capacity doing a cycle ergometer stress testing and the mean Watt/kg of these boys was 3.6. In Aandstad et al. (2006), 9 - 10 year old healthy Norwegian boys of normal weight achieved an absolute Watt mean values of 102 Watt which is far beyond the value gained by the 8 and 9 year olds in this study, indicating a higher physical performance capacity of our soccer athletes. In another study, by Ten Harkel et al. (2011), who investigated 12 – 18 year old healthy girls and boys of normal weight, a mean of

162 $Watt_{max}$ and 3.4 Watt/kg for boys was collected. Again, both values are far beyond the ones of our study, most probably for the above mentioned reason. While an average of 4.6 Watt/kg was achieved over all groups in our study, the $Watt_{max}$ collected by Ten Harkel et al. (2011) were similar to the $Watt_{max}$ of the second youngest group, the U12, of our study. In Bar-Or (1986, p. 379) values similar to the other studies for Watt/kg, 3.5–3.8, and for Watt absolute, 80–280, were found in 8 - 17 year olds.

In contrast to these studies and similar to our results, Gulmans et al. (1997), who investigated 77 participants aged 12 - 18 years, demonstrated on average 4.6 Watt/kg. As the participants were not specified as athletes but only as random sample of healthy and young males, these values seem to be quite high, especially regarding the performance values of the other studies of non-athletes. In fact, the values of non-athlete gained by Gulmans et al. (1997) were similar to the values of soccer athletes in our study. Furthermore, they also gained similar results regarding the peak performance within the different age-groups. In both studies, the youngest group showing little lower values than the others, the older age-groups, and these showing almost identical values. Though, the age of the participants of the youngest group in our study was 8 - 9 years and 12 years in the study by Gulmans et al. (1997) indicating, again, higher physical performances of the participants of our study.

Another indicator for aerobic fitness and physical power is VO_{2max}. Watt and VO_{2max} show an almost linear correlation and by means of certain formulas, VO_{2max} can be calculated out of Watt values of an exercise testing to exhaustion. Different formulas exist depending on the age of the participants, gender but also on the type of exercise test, treadmill or cycle ergometer.

Three different formula for the corresponding age-groups have been used in order to calculate average VO_{2max} and VO_{2max}/kg (Table 24).

Table 24: Illustration of VO_{2max} and VO_{2max}/kg for the age-groups, calculated with the corresponding formulas.

Age-group	Formula	VO_{2max}/kg	VO_{2max}
U10	$VO_{2max} = (12.44 \times Watt_{max} + 250)$	61.7	1829.9
U12	$VO_{2max} = (12.44 \times Watt_{max} + 250)$	64.7	2215.5
U14	$VO_{2max} = (11.87 \times Watt_{max} + 365)$	63.6	2798.4
U16	$VO_{2max} = (11.87 \times Watt_{max} + 365)$	58.8	3682.7
U18	$VO_{2max} = (11.35 \times Watt_{max} + 320)$	57.9	3906.6
Total		61.3	2886.6

Note: VO_{2max} values as medians in ml/min (VO_{2max}) and ml/min/kg body weight (VO_{2max}/kg). VO_{2max} and VO_{2max}/kg were calculated for each individual and medians for each age-group were calculated as illustrated. Total values were gained as the mean of the group values.
For the U18 the formula by Berg and Keul (1981), for the U10/12 and U14/16 two different formulas by Riddoch et al. (2005) have been used.

VO_{2max}/kg tended to decrease with increasing age (-groups) while absolute VO_{2max} increased with increasing age (-groups). If these values, especially the VO_{2max}/kg, are compared to the literature, one can see, that the values calculated in this study are higher than in most other studies. Labitzke and Vogt (1976) stated, that in trained children, VO_{2max}/kg can reach values of about 60ml/min.

However, in Ten Harkel et al. (2011) mean VO_{2peak} values of 47 ± 7 ml/min/kg were determined for 93 boys aged 8 - 18 years. VO_{2max} values between 2.04 - 3.56 l/min or 48 - 56 ml/min/kg in 12 - 18 year olds were measured in a study by Gulmans et al. (1997). Similar values were also found in Kolle et al. (2010) investigating healthy girls and boys aged 9 and 15 years of normal body weight. Even lower values for VO_{2max}/kg were investigated by Aandstad et al. (2006). In this study mean VO_{2max} of 45.9 ml/kg/min was gained in 9 and 10 year old healthy Norwegian boys of normal weight. This is far below the value gained overall groups in this study.

In contrast to our population, the subjects used in these studies were no athletes, which is most probably the major reason for the discrepancies in the maximal oxygen consumption values between these studies.

No restrictions can be made regarding the fact that in our study the VO_{2max} consumption was not measured but only calculated as this was done in some of the other studies as well.

Nevertheless, a summary of studies that used a cycle ergometer to measure VO_{2max} in males aged 9 - 14 showed reference values from 35.6 - 60.6 ml/kg (Freedson & Goodman 1993). These data also lie mostly beyond our values, though some of the mentioned studies also show similar values. Moreover, again, it has to be taken into account, that in our study, young athletes have been analysed.

Even though not directly comparable, VO_{2max} values gained in children and adolescents in treadmill exercise testings shall be shortly described here. The VO_{2max} values achieved in such stress testings, in comparison to cycle ergometer testings, like in our study, are on average 7 - 19% higher (Léger 1996). In a study by Fredriksen et al. (1998) relative VO_{2max} values from 53.7 - 59.7 ml/min in 8 - 16 year old healthy Norwegian boys were measured. Similar values of VO_{2max}/min/kg, 59.5 in 13 - 19 year olds and 55.0 - 60.5 in 8 - 17 year olds were gained in Nes et al. (2013) and Pettersen et al. (2001), respectively.
Considering the fact, that the values of the maximal oxygen consumption gained in this study are quite similar to the ones gained in other studies in which treadmill exercise testings were performed, it seems as if there was no 7 - 19% difference in peak performance between cycle ergometer and treadmill testings. However, again, it has to be taken into account, that in our study soccer athletes were investigated whereas in the other studies no athletes but just healthy individuals were used. Therefore it appears as if non-athletes doing a treadmill exercise testing can achieve VO_{2max} values of similar magnitude as athletes doing a cycle ergometer exercise testing.

4.1.5. Arterial Stiffness Parameters (PWV, AIx)

Although AIx and PWV correlate with each other (Marchais et al. 1993, Yasmin & Brown 1999), they are differently influenced by factors like gender and body height (Yasmin & Brown 1999). In fact, they are two different parameters of the properties of the arterial tree and cannot be used interchangeably (London et al. 2001, O'Rourke et al. 2002, van Trijp et al. 2004, Laurent et al. 2006, Vyas et al. 2007).

4.1.5.1. PWV

PWV is a powerful marker of arterial stiffness and in adults a surrogate marker for cardiovascular events (Laurent et al. 2001, London et al. 2004, Shinohara et al. 2004). Several studies have dealt with establishing reference values and threshold values (Khoshdel et al. 2006, Koivistoinen et al. 2007, Boutouyrie et al. 2010, Elias et al. 2011, Muller et al. 2013).

In adolescents and especially in children such data is scarce (Covic et al. 2006, Kis et al. 2008, Cseprekal et al. 2009, Kis et al. 2009) and large studies aiming at establishing reference values for PWV and threshold values for PWV and assessing the influence of anthropometric factors on it are largely lacking (Reusz et al. 2010).

One big problem in the measurement of arterial stiffness and the establishing of reference values and reference thresholds in children is, similar to blood pressure values in children, the fact that PWV is dependant of age and body dimensions (Kis et al. 2008, Cseprekal et al. 2009, Kis et al. 2009). As in children and adolescents huge differences in body dimensions can be found, uniform values are difficult to establish.

This is why in this study one of the aims was to expand the data and the knowledge on arterial stiffness and especially regarding reference values and threshold values in children. As the evidence available on this topic is inconsistent further investigations on this area are needed.

Therefore, also Reusz et al. (2010) had the aim to establish reference values for PWV in healthy children and adolescents of normal weight in accordance to body height and age. In this study percentile values for PWV for age and

body height were established and values between the 25th and the 75th percentile being considered as normal (Table 25).

Table 25: Percentile limits for PWV according to age in males. Values between the 25th and the 75th percentile a regarded as normal. (adapted by the author from Reusz et al. 2010)

Age	25th percentile	75th percentile
8	4.0	4.8
9	4.1	4.8
10	4.1	4.9
11	4.2	5.1
12	4.3	5.2
13	4.5	5.3
14	4.6	5.5
15	4.7	5.7
16	4.8	5.8
17	5.0	6.0
18	5.1	6.2

Note: Age in years, percentiles of pulse wave velocity (PWV) in m/s.

In comparison with these data, PWV values of our study are increased with an average PWV over all groups of 5.6m/s. In order to get a better comparability, PWV values of the participants of this study were categorized in percentiles regarding the study of Reusz et al. (2010).

Table 26 shows the percentiles for PWV values according to age and age-groups in our population. Still, higher PWV values in our study in comparison with the ones of Reusz et al. (2010) are obvious.

Table 26: Representation of the percentile limits for aortic pulse wave velocity of the participants of this investigation by age and age-groups.

Age-group	Age	Percentiles						
		5%	10%	25%	50%	75%	90%	95%
U10 (n=13)	8 (n=5)	4.4	4.4	**4.4**	**5.2**	**5.5**	-	-
	9 (n=8)	4.7	4.7	**4.9**	**5.2**	**5.5**	-	-
U12 (n=36)	10 (n=17)	4.4	4.6	**5.0**	**5.2**	**5.6**	5.9	-
	11 (n=19)	4.3	4.5	**4.8**	**5.0**	**5.4**	5.8	-
U14 (n=39	12 (n=18)	4.7	4.9	**5.2**	**5.4**	**6.4**	7.6	-
	13 (n=21)	4.8	4.8	**5.1**	**5.5**	**6.1**	6.5	7.0
U16 (n=47)	14 (n=30)	5.0	5.1	**5.4**	**5.9**	**6.1**	6.8	6.9
	15 (n=17)	5.3	5.3	**5.3**	**5.7**	**6.5**	7.7	-
U18 (n=37)	16 (n=11)	5.2	5.2	**5.4**	**6.1**	**6.5**	7.5	-
	17 (n=24)	5.5	5.2	**5.7**	**6.0**	**6.8**	7.6	15.4
	18 (n=2)	5.8	5.8	**5.8**	**7.1**	**-**	-	-

Note: Due to the little “n“ in certain ages, no 90th, 95th or 75th percentile could be estimated. Age in years, percentiles of pulse wave velocity values in m/s.

One possible explanation for these discrepancies is the use of different devices. Although the usage of both devices, the one in the study by Reusz et al. (2010) as well as the one used in this study have been justified per se, the comparison of, from these gained values, may still be problematic.

Though, established PWV values of healthy women by Muller et al. (2013) were in accordance with the ones by Reusz et al. (2010) indicating the comparability of different devices. In another study (Sakuragi et al. 2009) in which the influence of adiposity and physical activity on arterial stiffness was assessed, mean PWV for 10 year old normal weight boys and girls was 4.2m/s, again being beyond the values of this study and in accordance with the ones in Reusz et al. (2010).

Even lower PWV values of aortic PWV in 10 year old boys with 2.6m/s were measured by Schack-Nielsen et al. (2005).

Nevertheless, the similar results of most of the before mentioned studies, which did not use the same device, but still demonstrating similar PWV values, indicate that for the assessment of PWV and the comparison of these values, the usage of different devices might not play an important role. Furthermore it emphasises the apparently influence of physical activity and regularly physical training on the arterial stiffness.

In a study by Hudececk (2014) of our working group, the same procedure, method, stress protocol, cycle ergometer and arterial stiffness device like in our study was used in untrained children aged 11 - 13 years (unpublished data). PWVao Pre as well as PWVao Post and ∆PWVao values were smaller than in our study, indicating that the device and/or method appears not to be the reason for the differences in PWV values. Therefore, the possible influence of the training in soccer athletes, as explanation for the higher values receives new nourishment because in our study soccer athletes were investigated while in the other studies only normal physical active individuals were investigated.

However, different methods and devices are a potential source for differences in parameter values.

Although the here mentioned studies were conducted in different nations and even continents (Sakuragi et al. 2009) differences in PWV values due to this fact are not likely. Reusz et al. (2010) showed no significant differences in PWV between participants of Hungary, Italy and Algeria.

4.1.5.2. AIx

As already mentioned, the cardiovascular system with all its components is a complex and finely tuned system. Neither only the peripheral, nor only the central arteries but the whole arterial system contributes to the timing and amplitude of wave reflection and therefore AIx (Edwards & Lang 2005). Whilst the large arteries buffer the pulsatile blood flow, the muscular arteries are able to alter the travel speed of the pressure wave and the arterioles serve as the main sites of reflection of the pressure wave (Nichols & Edwards 2001, Safar et al. 2003).

However, in order to be able to interpret AIx, reference values for AIx are needed (Laurent et al. 2006). A literature search revealed only few studies that offer suchlike.
For men, Mitchell et al. (2004) postulated threshold values for AIx of 33% and Wojciechowska et al. (2006) postulated for peripheral AIx 90% and 30% for central AIx as threshold values for being normal.

For children, however even fewer reference values for AIx can be found in literature. As for this, our ascertained data serve as important reference values for children and adolescents. Furthermore, with this lack of literature, we can only compare our AIx values of young, healthy, male soccer athletes to these of adult non-athletes and to one study by Lowenthal et al. (2014) who investigated AIx and PWV in healthy children and adolescents aged 10 - 19 years. In comparison to the latter study which gained an average AIx value of 3.06 ± 9.51% only the U18 of our investigation showed lower values. However, due to large standard deviations no significant differences are at hand.

In comparison to the reference values for adults, in our study the median values within each group as well as over all groups were lower. However, the huge standard deviations have to be considered. Only in the U10 and the U12 none of the participants had Pre AIx values above 30%. Further, these two groups had the smallest standard deviations which may be due to the smaller "n" in these groups in comparison to the other groups. Despite the problem of the mentioned standard deviation in the groups, AIx tended to decrease with increasing age (-groups) at rest. In fact, only the U12 and the U16 and U18, respectively, showed significant differences. The decreasing AIx with increasing age (-groups) is contrary to literature but in accordance with studies (Smulyan et al. 1998, Nurnberger et al. 2004, Shimizu & Kario 2008, Weber et al. 2008), which found negative correlations of AIx with body height. Although other studies demonstrated increases in AIx with increasing age (Mitchell et al. 2004, Nurnberger et al. 2004, McEniery et al. 2005, Weber et al. 2008, Janner et al. 2010), this only counts for adults, as the age-related increase in PWVao and central arterial stiffness are responsible for the increase in AIx in this population, and therefore might not be the reason in our study. That means, that in our case, the increasing body height, accompanied by increasing age rather than the increasing age per se might be the reason and responsible for the decreasing AIx with increasing age (-groups).

In Post values of AIx, no consistent values were gained. Even higher standard deviations than in Pre values prevent interpretations and prevent possible relationships with other factors and parameters.

4.2. Differences

4.2.1. Differences in Parameters between Pre and Post Values over all Groups

In all blood pressure parameters, systolic, diastolic, mean arterial pressure, pulse pressure and aortic systolic blood pressure, as well as in heart rate and PWVao significant differences, and more precisely increases, were found between Pre and Post values indicating an influence of the ergometry to exhaustion on these parameters.

For blood pressures and heart rate, this is nothing new, as the cardiovascular system has to undergo certain adaptations in order to fulfil the physical and metabolic demands due to the stress testing.

The time between finishing the ergometry and the Post blood pressure measurement was only around three minutes and therefore too short to allow the organism and the cardiovascular system a complete recovery and decrease to resting values. For this reason, HR Post and blood pressure Post values were still above the Pre values and within normal, expected physiological ranges.

Normally, in a healthy cardiovascular system and organism, systolic blood pressure shows higher increases than diastolic blood pressure does due to physical loads. In fact, due to a complex interplay of factors like cardiac output and peripheral resistance, diastolic blood pressure mostly stays unchanged while systolic blood pressure increases (Alpert & Fox 1993).

Whilst diastolic pressure shows only little alterations and can either decrease or increase (Bar-Or 1986, p. 35), mainly dependant on the peripheral ventricular width, the increase in the systolic blood pressure is mainly due to the increased contractility of the myocardium. In this process not only the systolic intraventricular pressure changes but also the peripheral systolic pressure.

Physiologically, the systolic pressure increases proportionally to the increase in workload and metabolic turnover (Eriksson & Koch 1973).

In children, both pressures increase to a lesser extend in contrast to adolescents (Strong et al. 1978, Kulangara & Strong 1979,Riopel et al. 1979, James et al. 1980) which is due to a smaller cardiac output per minute and stroke volume. Furthermore, in children, smaller and shorter peripheral vessels also account for a lower peripheral resistance and therefore causing a lower blood pressure (Bar-Or 1986, p. 35).

With increasing systolic blood pressure and roughly steady diastolic blood pressure, as a result of physical loads, in contrast to the situation at rest, and independently of whether measured in children and adolescents or in adults, the difference between these two pressures widens and hence resulting in an increased PP, explaining the differences between Pre and Post values in PP.

Independent of where systolic blood pressure is measured, peripherally or centrally, systolic blood pressure increases as a result of increased physical load. Thereby, like at rest (Wilkinson et al. 2000, Schillaci & Grassi 2010), central systolic blood pressure demonstrated values below the peripheral values (Table 8). In fact, systolic blood pressure increases due to a physical stress, independently of the region in the vascular system, with the central pressure lying beyond the peripheral ones.

Although, for heart rate and the blood pressure parameters being influenced by physical activity and a stress test is nothing new, for PWVao this is nothing that is sufficiently described in the literature. Several studies (Sugawara et al. 2003, DeVan et al. 2005, Heffernan et al. 2006, Casey et al. 2007, Tabara et al. 2007, Cortez-Cooper et al. 2008, Hayashi et al. 2008 ,Kawano et al. 2008) have focused on long-term effects and even on acute effects of different sport exercises on arterial stiffness but there is hardly any evidence to be found investigating the difference between PWVao values at rest and values during or directly after exhaustion and therefore investigating the influence of physical activity to exhaustion on arterial stiffness and the changes it causes in the cardiovascular system.

PWVao values over all groups almost doubled from Pre to Post measurement, which means, that even around three minutes after the ergometry was finished, the speed at which the pressure wave travelled through the central system was almost twice as high as at rest indicating stiffer central arteries than at rest.

Although not numerous, reference values for PWVao at rest for adults can be found in the literature. For children even fewer data can be found, as has been discussed above. Nevertheless, for PWVao reference values directly after an exercise to exhaustion no such data can be found. Therefore the Post PWVao values of young soccer athletes in this study cannot be compared with others.

Sadly we do not have PWVao values at the peak of the exhaustion but only three minutes after the cycle ergometry to exhaustion was finished. It would be very interesting to see how much more PWVao can be increased, if at all.

In conclusion, the revealed increases in blood pressure parameters, heart rate as well as PWVao indicate that these parameters were influenced by the physical load in the form of the cycle ergometer stress testing.
Furthermore, for PWVao, the increase means an acute higher central arterial stiffness due to the physical load. A similar result, an increase in central arterial stiffness and an increased PWVao was found by DeVan et al. (2005) who investigated the acute effects of a resistance training on central arterial stiffness in healthy adults aged 23 – 35 years. Another study investigating the acute effects of a resistance training on arterial stiffness in healthy young adults found no changes in central arterial stiffness (Heffernan et al. 2006). Acute effects of endurance training on arterial stiffness demonstrated different results with no changes in central arterial stiffness in healthy young women and men (Sugawara et al. 2003, Heffernan et al. 2007b) or increases in the distensibility of the central arteries in healthy males (Kingwell et al. 1997a). Consequently, our results are different to other studies where no changes or decreases in central arterial stiffness and PWVao were found.

In contrast to PWVao, in AIx no significant differences between Pre and Post were found (analysed by Wilcoxon) which would indicate that on this parameter the ergometry to exhaustion and the physical load involved have no influence. However, this is not true and a result of the huge standard deviations of this parameter. This could be confirmed by the ANOVA with repeated measures, more exactly, by the significant time effect (see chapter 3.2.4.2.). Therefore, the statement that AIx as a parameter of systemic arterial stiffness seems not to be changed or affected by such an exercise stress load is not true.

4.2.2. Differences in Pre Parameter Values between Groups

Significant differences between the groups in Pre values were found for PWVao, AIxao, HR and blood pressure parameters.

PWVao values were highest in the oldest group and showed to be significantly different to the three youngest groups. Moreover, the PWVao values of the second oldest group differed significantly from the U12 but not from the U10. Even though

differences between the U10 and U12 were only poor, they were still enough for the U12 but not the U10 do be significantly different from the U16.
These facts, indicate that the age might play an important role in PWVao values at rest. In fact, it is well-known that in adults central arteries get stiffer and PWVao increases when getting older. Furthermore, some studies have shown increases in PWVao in children and adolescents as well (Reusz et al. 2010, Hidvegi et al. 2012).
Nevertheless, in children and adolescents different factors might contribute to increases in PWVao in these ages than do in the elderly.

As we investigated young athletes, “trainings age” and physical performance capacity rather than “biological age” might contribute and/or be a reason for higher PWVao values in the older groups. Athletes of the U18 have been training for more years than the U10 or U12 or U14 and therefore showing a relatively higher PWVao as a result of an increased arterial stiffness. This would mean negative effects of a regular soccer training regarding vascular properties and therefore would lead to the conclusion that, in order to prevent the stiffening of the arteries in these young years, not to be physically active.
In order to falsify or to verify this conclusion, non-athletes of this age should be investigated in a similar intervention in order to see whether in these also an increase in PWVao can be found. On the other hand, as other studies have shown increases in PWVao in these young years even in non-athletes, this increase might be a result of growing up and biological age. Moreover, it might be that puberty constitutes a turning point in these parameters.

In AIx the two oldest groups showed significant differences to the U12 but not to the youngest group, the U10. Like in the chapter before this indecisive result might be a result of the huge standard deviations. Nevertheless, an important determinant of AIx is body height. As in a tall person distances between arterial regions are larger, and the reflected wave needs relatively longer, for the same PWV, to reach the ascending aorta, taller persons have lower AIx values than smaller persons (McGrath et al. 2001, Janner et al. 2010), accounting for example for the average higher AIx in women, and therefore explaining the lower and significantly different values of AIx in the older groups in comparison to the younger groups in our study.
Nevertheless, some authors state, that body height alone might not be the reason for different AIx values between the sexes and demonstrated differences between

women and men even after adjusting for body height (Gatzka et al. 2001, Mitchell et al. 2004, Kohara et al. 2005, Fantin et al. 2007). Some of them argue that the differences may not be due to arterial stiffness per se but due to differences in wave reflections (McEniery et al. 2005).

HR Pre values showed significant differences between the U18 and the three youngest groups. Also the U16 and the youngest group, the U10, differed significantly. These differences between the youngest groups and the oldest groups could be explained by the fact, that the older the participants were, the longer they have already been training and therefore the more trained their organism was resulting in a lower HR at rest. A reduction in heart rate at rest as a result of endurance training is a well-known phenomenon and has been shown in several studies (Carter et al. 2003, Huang et al. 2005, Yilmaz et al. 2013). Furthermore, the lower HR Pre values in the older subjects could be a result of them being more common to the procedures in comparison to the younger subjects who were not so experienced in the examinations and probably did them for the first time.

Likewise, the significant differences in systolic and mean arterial pressure between the two youngest groups and the three oldest groups, respectively, indicate an increase in these parameters with age, either biological or trainings age, or the physical performance capacity and fitness status. As physical activity and especially endurance training is associated with decreases in systolic blood pressure (Tsai et al. 2004, Collier 2008) and as blood pressure is dependent of body height and increases during growth (Falkner & Daniels 2004) higher systolic and mean arterial pressure in the older groups are more likely the result of biological age rather than trainings age or physical performance capacity.

In diastolic and especially in pulse pressure, different and not that decisive results were found.

4.2.3. Differences in Post Parameter Values between Groups

The following parameters measured Post ergometry showed significant differences between the groups: PWVao, HR and blood pressure parameters but not AIxao. Again, for the latter this was due to the huge standard deviations.

In Post PWVao, similar results as for Pre PWVao were found. Again, there was an increase from the youngest to the oldest groups in the values with the two youngest groups being significantly different from the three oldest (Table 16).
PWVao values directly after an ergometry to exhaustion have, to our knowledge, not been investigated so far. Therefore our values constitute new knowledge regarding the behaviour of PWVao and arterial stiffness.

Like in rest values, Post values of PWVao demonstrated increases with increasing age. In contrast to the values at rest, here the influence of the exhaustion load has to be taken into account. There are several possible reasons for the Post PWVao values being higher in the older individuals in contrast to the younger ones. First, this could be due to normal changes in physiology during the process of growing up. It might be that PWVao Post values, like values at rest, increases with increasing age. Several studies describing PWVao values at rest in children and adolescents demonstrated increasing PWVao values even in this young ages (Reusz et al. 2010, Hidvegi et al. 2012) which might be true for Post values as well. Second, it could be due to a higher training status and longer years of training. The more trained one is, the higher PWVao Post is or the older one is the higher is the PWVao and therefore the arterial stiffness. Third, it could be due to greater exhaustion of the older participants, as a result of greater motivation and wish to accomplish higher loads. Also a better understanding of what the purpose of such a screening and investigation is might lead to greater exhaustion and therefore greater PWVao Post values in older groups.
Regardless of what the reason for higher PWVao values might be, it means that the speed at which the pulse wave travels though the central arterial system is higher, indicating a higher arterial stiffness.

In HR significant differences were found between the U10 and all other groups as well between the U12 and the U14 and the U18, respectively. When compared to the HR_{max}, HR Post, in percent of the HR_{max}, tended to increase with increasing

age (-groups) (Table 6). This could mean, that the older subjects needed longer to recover from the ergometry, or that the younger participants did not exhaust themselves to the same degree as the older participants.

In all blood pressure Post parameters, values tended to increase (Table 8). Significant differences in all parameters between the groups were found mostly either between the youngest two groups and the other groups or between the oldest two groups and all the younger groups. Together, differences were mostly found in an chronologically order which means that with increasing age and or physical performance due to trainings age, values increase and eventually become significantly different to the values of the younger groups. Maybe puberty, which occurs around 12 - 14 years and which is a critical period during which numerous physical as well as psychological changes take place, is responsible for these differences. Therefore, puberty and changing physiological, hormonal and metabolic situations might be the reasons for differences between the younger and the older groups, primarily seen.

Of course these facts also might be true for the other parameters and not only for blood pressure parameters.

4.2.4. Differences of Changes in Parameter Values due to the Intervention between the Groups

In this chapter only PWVao and AIxao are going to be discussed, because these are considered the parameters reflecting the conditions of local and systemic arterial stiffness the best.
As one major goal of this study was to find out about the behaviour of arterial stiffness within the scope of a physical load to exhaustion, PWVao and AIxao were thought to be the best parameters describing these effects.

4.2.4.1. PWVao

In PWVao values, differences between groups were found regarding the changes from Pre to Post values. In fact, the two youngest groups (U10, U12)

significantly differed from the three oldest groups (U14, U16, U18), respectively, indicating differences in the changes from Pre to Post between the older and the younger groups. This alone does not give information about magnitude or direction of these changes. Therefore the differences in mean values can help. In all groups increases in PWVao values from Pre to Post were demonstrated which indicated differences only in magnitude but not in direction between the groups.

The differences between the Pre values and the Post values were calculated as ∆PWVao and represent the magnitude of the change between Pre and Post values.

4.2.4.1.1. ∆PWVao

As the calculation and analysis of ∆PWVao revealed, the two youngest groups demonstrated the lowest increases in PWV from Pre to Post whereas the three oldest groups demonstrated the largest increases. In fact, ∆PWVao increased from the U10 to the U18 with every group, except for the U18 which showed values slightly beyond the ones of the U14. Therefore significant differences were only found between the U10 and U12, respectively, and the U16, which showed the largest increase. Furthermore a significant difference in ∆ of PWVao was found between the U10 and the U18. Although the U18 demonstrated only the third largest increase in PWVao, still a significant difference to the U10 with the smallest increase in PWVao was demonstrated. The fact that the U14 showed higher standard deviations than the U18 resulted in the U14, despite higher PWVao increase in contrast to the U18, not to be significantly different from the two youngest groups.

Nevertheless the magnitude of the increase or the steepness of the increase, expressed as ∆PWVao, demonstrated a different hierarchy regarding the age-groups with increases in ∆PWVao from the U10 to the U12 to the U18 and finally the U14 and the U16. Therefore the greatest steepness of ∆PWVao or the largest increases in PWVao from Pre to Post was demonstrated in the U16.

Taken together, PWVao increased in all groups from Pre to Post. The differences between Pre and Post PWVao values were significant in each group.

Not only in Pre PWVao but also in Post PWVao, values increased from group to group, being lowest in the youngest and highest in the oldest group. As a result, the U10 demonstrated the lowest PWVao Pre as well as Post values and the U18 demonstrated the highest PWVao Pre and Post values with the other groups lying chronologically in-between them.
Therefore, it seems that with increasing age, even in such young years, the arterial stiffness increases not only at rest but also due to a physical stress load.
At rest, this increase can only be a result of physiological changes during the process of aging or of the influence of long-term training. Still, it has to be considered, that participants of younger groups have been training for a proportionally shorter period than participants of the older groups. Therefore training induced adaptations might be proportionally smaller in younger groups. In order to find out about this, further investigations which compare athletes with non-athletes of that age in a similar manner are needed.

Independently of the overall higher PWVao values at rest of this study (see chapter 4.1.5.1.) in contrast to other studies, increasing PWVao values within these ages has been demonstrated by others (Reusz et al. 2010, Hidvegi et al. 2012).

While at rest, a higher PWVao and arterial stiffness is regarded as negative in terms of cardiovascular diseases as well as overall mortality and morbidity (Meaume et al. 2001, Mattace-Raso et al. 2006, Willum-Hansen et al. 2006, Inoue et al. 2009, Mitchell et al. 2010), higher values under load and during physical exercise might be the result of or the requirement for physical training and better performance. This is similar to heart rate for example, where lower values at rest are considered with higher training status with no alterations in maximal heart rate. In fact, a lower heart rate at rest and unchanged maximal heart rate enlarges the range of the heart rate and therefore increases the adaptability to different loads.
Likewise, in PWVao, unchanged values at rest and higher maximal values increases the range of PWVao and the arterial stiffness and therefore the adaptability of the central arteries to certain loads and strains. Even if PWVao values at rest are increased in athletes, as it might be in our study, the range

of PWVao and the adaptability of the central arteries might still be increased when maximal PWVao shows an even greater increase.

Again, this possible increase in the adaptability of the arterial system might be the result of physical training or the requirement for it. Furthermore, the increasing adaptability of arterial stiffness and PWVao, expressed as ∆PWVao, with increasing age (-groups) might be the result of the older groups having been training for a longer time or the result of still changing physiological parameters during the process of growing up and as a result of puberty.

4.2.4.2. AIxao

In contrast to PWVao, in AIxao ANOVA revealed only differences in effect of time. This means that AIxao values between Pre and Post were significantly different and that these differences cannot be connected to age (-groups).
As AIx is a complex parameter which is influenced by many factors like heart rate, gender, body height and PWVao, defining the time at which the reflected wave reaches the ascending aorta, but also age and blood pressure/peripheral resistance (Wilkinson et al. 2002, Nurnberger et al. 2004, Shimizu & Kario 2008, Weber et al. 2008, Janner et al. 2010), it is difficult to interpret these results. Furthermore the inconsistent trends without any apparent tendencies of the AIx Post values do not allow any conclusions

4.2.4.2.1. ∆AIxao

Due to the problem of huge standard deviations as well as indecisive mean values within the different age-groups no further interpretations regarding ∆AIxao can be made.

To our knowledge no literature exists using AIx in order to describe systemic arterial stiffness past a physical load. As this parameter is influenced by several factors like heart rate, blood pressure/ peripheral resistance and PWV, parameters which are influenced themselves by physical loads, AIx seems not to be suitable in this context. While in Pre conditions AIx can be used in order to describe the systemic arterial

stiffness of an organism, in post exercise conditions and in the context of physical loads AIx seems to be useless.

In further investigations, it may be interesting to find out about different corrections in AIx like for heart rate or blood pressure in order to gain useful information.

4.3. Correlation Analysis

So far, parameters describing cardiovascular conditions like PWVao, AIxao, blood pressure parameters as well as heart rate have shown to be influenced by the ergometry to exhaustion. Nevertheless, it is important and interesting to know whether these parameters and physiological systems show similar directions of change, similar dependencies of one another or are otherwise (in-) dependent of each other.
Therefore correlation analyses have been made over all groups but also within the groups.

4.3.1. Correlation Analysis over all Groups

Over all groups, PWVao values like PWVao Pre, PWVao Post and ΔPWVao as well as AIxao Pre demonstrated significant correlations with different other parameters.

The first obvious correlation demonstrated PWVao at rest (Pre) being positively correlated with age. This means that the older the individual was the higher was the arterial stiffness. Already mentioned in chapter 4.2.2., this was interesting as it showed that even in such young years PWVao and arterial stiffness shows an increase. This is well-known for the process of aging from young adults to elderly (Koivistoinen et al. 2007, Merrill et al. 2011) and, as some other studies have shown too, already starts at this period of age (Reusz et al. 2010, Muller et al. 2013). However, in this age other mechanisms rather than structural changes due to a loss of elastin and increasing collagen might be responsible, as these take considerable time to occur (Lakatta 2002).
The dependency of Pre PWVao of age in this population might be a result of normal physiological changes during the process of growing up as well as of training induced physiological changes. Even both factors together might explain this correlation.
PWVao Pre demonstrated to be negatively correlated also with AIxao Pre indicating that a higher PWVao at rest results in a lower AIxao at rest. This is in accordance with literature (Marchais et al. 1993, Yasmin & Brown 1999). When PWVao increases, independent of the reasons for that, it means that the reflected retrograde pressure wave reaches the ascending aorta and the heart

earlier, in the late systole instead of the diastole, and therefore increases the central aortic systolic pressure and the augmentation pressure (McGrath et al. 2001, Janner et al. 2010). Due to the increased augmentation pressure, AIxao also increases.

PWVao Pre was also significantly and positively correlated with the achieved Watt absolute. The more Watt absolute could be overcome by the participants, the higher PWVao at rest was. This means, that the fitter and stronger and therefore the better trained the individual was, the higher was also its PWVao at rest. This could explain the higher PWVao values at rest in comparison with reference values of other studies (see chapter 4.1.5.1). In these studies children and adolescents of similar ages had lower PWVao values at rest. However, the participants of these studies were no athletes. Therefore it might be that in children and adolescents regular sports exercise increases PWVao at rest, although it has been shown to be the other way round in adult athletes. In fact, while in adults, studies have shown that endurance training decreases PWVao at rest (Otsuki et al. 2006, Sugawara et al. 2006, Collier et al. 2008), in children and adolescents, until a certain age, it might be different. It could be that, as a result of the training, the PWVao Pre increases, explaining the higher PWVao values in combination with higher Watt performance in young athletes in contrast to non-athletes. If so, there should be a difference between the younger groups and the older groups which should have proportionally higher PWVao Pre values as they have been training for several years in contrast to the younger ones. In fact, the U18, the oldest group, demonstrated significant higher PWVao Pre values as the three youngest groups, respectively (see chapter 3.2.2, Table 14). Therefore, one could argue that in children, training is the reason for the higher PWVao at rest values in comparison with other studies. However, the higher PWVao values in the older groups can also be the result of them being older and therefore of a normal physiological change during the process of aging and growing. In order to verify this explanation, it would be necessary to investigate endurance-trained as well as non-athletes in these age-groups in a similar study design in order to compare these results.

Another explanation for the higher Pre PWVao values could be the usage of different measurement devices in our and the other studies although the investigation by Hudececk (2014), mentioned before, using the same device as in this study negates this explanation.

PWVao values at rest were also positively correlated with PWVao after the ergometry to exhaustion (Post) indicating that the higher PWVao at rest are, the higher the PWVao values after the ergometry will be and vice versa. This could mean that there might be some kind of physiological range of PWVao independent of the “net” PWVao values. If one has, for some reason, higher PWVao values at rest, one will also have higher Post values and if another person with similar state of fitness and condition has lower Pre values it will also have lower Post values. Therefore, both values could go hand in hand and presuppose each other, maybe as a result of biological or trainings age.
It might also be that in order to achieve a trainings-induced high performance capacity, a certain range of PWVao is necessary. Values above as well as beyond this range may not be optimal in this context. Higher values maybe correlated to certain disease states and lower values maybe correlated with a low trainings status. Due to different physiological conditions in children in contrast to adults, suchlike ranges might not be possible at that age indicating smaller PWV ranges although being highly trained.

Further similar correlations like in PWVao Pre were found in PWVao Post. Post values correlated positively not only with Watt absolute, but also with Watt/kg. The fact, that both, Watt absolute and Watt/kg, were correlated with PWVao Post underlines an even stronger connection between the fitness state and the Post PWV as a correlation with only Watt absolute. As in the study population individuals had normal BMI’s corresponding to their age, achieved Watt absolute has good power indicating a relationship between one’s fitness and performance capacity and the PWVao. Nevertheless, Watt/kg has an even stronger statement as it is independent of the body stature. Therefore higher Watt/kg being correlated with higher PWVao Post strongly indicates that the fitter, stronger and better trained an individual is, the higher is the PWVao Post. It might be that a higher PWVao Post is needed in order to achieve greater performance. This would mean that only individuals with higher PWVao Post values, more exactly individuals whose organism and vascular system is able to produce such high values, might be able to achieve higher Watt performances. On the other hand, it might be that a higher PWVao Post is the result of greater performance and achieved with extensive training as kind of functional and physiological adaptation to sports training.
Age, again, demonstrated also to be positively correlated with PWVao Post. Same explanations like for PWVao Pre could be true. Biological age as well as

trainings age might be the reason for increased PWVao Post values with increasing age.

Last but not least, PWVao Post showed, like PWVao Pre, significant, negative correlations with AIxao at rest (Pre) meaning that even higher PWVao values after exhaustion are based on even lower AIxao vlues at rest. Despite the fact, that AIx is a parameter influenced by several factors, lower values of AIx are considered as good in contrast to higher values. As increased AIx has been proven to independently predict the risk for cardiovascular diseases and mortality, lower values indicate a lower risk regarding these disease states (Wang et al. 2010, Cho et al. 2013). On the other hand, higher PWVao Post values may account for an adaptable aorta and central arteries. Hence, a correlation between these two parameters could be interpreted as a testimony for a flexible, healthy adaptable cardiovascular system. Furthermore, as AIxao is a marker for systemic arterial stiffness, a decreased AIxao correlating with increased PWVao Post suggests a wide range of the vascular system regarding its stiffness and therefore indicates a large adaptability of this system.

The last PWVao parameter, ∆PWVao, also demonstrated some interesting correlations, similar to PWVao Pre and Post. First, ∆PWVao correlated positively with age which means that the older one was, the larger was the difference between PWVao Pre and PWVao Post values. This difference, or the ∆ of PWVao represents the adaptability or the physiological range of PWVao and the arterial stiffness and might, again, be a result of biological age but also trainings age. Therefore, the better trained one is and the more years of training one has, the bigger its adaptability of the central arteries and their stiffness might get. On the other hand, only the fact of getting older and becoming an adult might increase the physiological range of PWVao and arterial stiffness until, maybe, being an adult and reaching a final range. If the biological age but not the trainings age determines the range of PWVao, similar PWVao ranges for both, non-athletes and athletes in our study should be found.

Of course there is always the possibility of a mixture of influences, which has to be considered. Nevertheless, data for non-athlete children regarding these research questions are needed and should be investigated in a next study.

∆PWVao also showed correlations to Watt absolute and Watt/kg. Similar explanations like for PWVao Post may be correct for ∆PWVao as well. A wider range and a higher ∆PWVao could be the result of physical activity in trained individuals. It might also be that, a wider range and higher ∆PWVao are the

requirements for intensive, regular, expedient training and as a result greater performance and greater achieved Watt absolute and Watt/kg.
Another interesting strong correlation with ∆PWVao demonstrated PWVao Post indicating that the higher Post PWVao values are, the greater the ∆ in PWVao is. This means that not PWVao Pre but PWVao Post values are responsible for a greater ∆PWVao. Therefore, again, only PWVao Post values and not PWVao Pre values, which, in contrast to the Post values, stays proportionally more stable, define a greater ∆PWVao. The PWVao values at rest may constitute threshold values at a physiological border and therefore are quite stable. The PWVao Post values on the other hand are quite changeable and may be influenced by a number of different parameters. The system of the arterial stiffness and its possible range of PWVao might therefore be upwards open.
A final negative correlation of ∆PWVao was found with AIxao Pre indicating that the larger the difference in PWVao between Pre and Post values were, the lower the AIxao at rest was. Similar to what was mentioned above, a decreased AIxao at rest correlating with a larger ∆PWVao, hence increased range of aortic adaptability regarding the arterial stiffness, seems to be accompanied by a reduced systemic arterial stiffness at rest. The latter could therefore be the result of a wider ∆PWVao or the requirement. Moreover, both could be the result of physical activity and/or be mutually dependent of each other.

At last, AIxao Pre but not Post was correlated with other parameters, of which two, PWVao Pre and ∆PWVao, have already been discussed above. Furthermore, the correlation between AIx and PWV is one, that has also been found by other authors (Marchais et al. 1993, Yasmin & Brown 1999).
Another parameter was age which demonstrated a negative correlation with AIxao. This means that the younger one is, the higher AIxao at rest will be or the older one is the lower is the AIxao at rest. Evidence has demonstrated, that AIx increases with age (Wojciechowska et al. 2006, Fantin et al. 2007, Weber et al. 2008, Janner et al. 2010) which stays in contrast to the correlation found here in this study. Nevertheless, increasing AIx values with increasing age only counts for adults and the process of aging, as arteries get stiffer when getting older and therefore causing a higher AIx. However, in children and adolescents of this age-groups, still being in the process of growing, something different might be the reason for this correlation. As the younger participants of this study are also the smaller ones, the seen correlation might in fact be a correlation between body height and AIxao. As described before, the smaller a person is, the faster the

reflected, retrograde pressure wave reaches the ascending aorta, resulting in an increased AIxao (McGrath et al. 2001, Janner et al. 2010). In fact, after analysing the data and preparing the discussion of this study a subsequently correlation analysis regarding body height and AIxao Pre was done. This analysis revealed a significant negative correlation ($p<0.000$; $\rho=-0.482$) between body height and AIxao Pre over all groups, confirming our assumption.
Another possible explanation for the negative correlation between AIxao Pre and age could be, that the less trained one is the higher AIxao Pre is, as the higher AIxao values at younger ages might be due to fewer years of training. This would mean that a higher trainings status and longer years of training in this population decreased systemic arterial stiffness.

Furthermore, Watt absolute demonstrated a negative correlation with AIxao Pre. The more Watt absolute were achieved and the stronger one was the smaller were the AIxao Pre values. As mentioned before, AIx is a marker for systemic arterial stiffness and decreases in AIxao mean decreases in systemic arterial stiffness. A healthy and high-performance organism is able to render high physical performance, master high loads and achieve more Watt absolute during a cycle ergometer stress testing.
Furthermore, a reduction in systolic blood pressure and even in diastolic blood pressure is the result of physical activity and especially endurance exercise (Otsuki et al. 2006, Sugawara et al. 2006, Collier et al. 2008). Functional alterations in the vascular system are accompanied by abnormalities in blood pressures which has been described in adults as well as in children (Lurbe et al. 2012) and central arterial stiffness increases as a result of increased central blood pressure (O'Rourke et al. 2002). The other way round is also possible, describing the crosstalk of these factors. Therefore it is not devious that it may happen the other way round and that a reduced blood pressure goes hand in hand with a decrease in arterial stiffness and vice versa. Therefore, a reduced systemic arterial stiffness is plausible to be correlated with higher physical performance capacity and more achieved Watt absolute. Although it would be possible that lower AIx is a result of higher performance capacity due to progressive physical training, it might also be the requirement for the latter and increased physical performance.

4.3.2. Correlation analysis within the groups

When correlations were analysed for parameters within the age-groups fewer consistent, strong correlations, like for over all groups were found.
In fact, the only constant correlation that was found in each of the groups was between ΔPWVao and PWVao Post, a correlation that was also found over all groups.
Once again, this indicates, now also for the different age-groups, that the higher the PWVao Post value was the larger the Δ between the Pre and the Post PWVao was. Thus, PWVao Pre seems to have only minor influence on ΔPWVao.

The fact that within the groups only a few correlations were found might be due to smaller collectives.

5. Conclusions, and perspectives

To our knowledge, this is the first study investigating the acute effects of a physical exercise to exhaustion in children and adolescents. In particular, healthy, male soccer players aged 8 – 18 years were investigated doing a cycle ergometry stress test to exhaustion and were analysed in age-groups according to the youth squads of their soccer club.

The aims of this study were to investigate reference values for PWV and for AIx at rest as well as following an exercise to exhaustion for this population. Furthermore, possible influences and changes due to different ages but also due to different levels of training status and therefore different physical performance capacities should be assessed.

The final aim of this study was to find out about possible correlations between parameters of arterial stiffness, physical workload capacity and aging.

PWV values at rest, in comparison with other studies, demonstrated to be increased. In comparison to these studies, which investigated non-sportive healthy children and adolescents, the participants in our study were soccer athletes. Furthermore, in children and adolescents no studies investigating athletes could be found. An increase in PWV values at rest was surprising, as in adults, several studies have demonstrated decreases in arterial stiffness as a result of endurance training. However, soccer is not a pure endurance sport. Similar to other sports which constitute a mixture of resistance and endurance training, for example rowing exercise, a decrease in arterial stiffness values may not be as pronounced as in endurance sports or even increased. This may be an explanation for the higher PWV values at rest in this study in comparison to other studies. Still, another explanation could be that in children and adolescents, influences of physical training could be different. Nevertheless, our hypothesis that in children, like in adults, PWV values are decreases in comparison with non-athletes as a result a regular physical training has to be rejected.

PWV Pre values but also PWV Post values demonstrated increases with increasing age (-groups) which is in agreement with reference values for healthy non-athletes of that age (at least for the Pre values). As our Post PWV values constitute new scientific data for this kind of population it could only be compared to data of studies of submaximal PWV values in adults. Furthermore, the ΔPWV values demonstrated to be increased with increasing age (-groups) indicating an influence of biological age and/or trainings age and physical performance capacity. Therefore, our hypothesis that the arterial stiffness experiences alterations and changes due to a physical exercise can be confirmed.

Furthermore, correlation between PWV, AIx and parameters of the physical performance capacity could be found in this study. As we investigated soccer athletes, the participants of our study showed, in comparison to non-sportive children and adolescents, higher physical performance capacity, measured in Watt. While absolute Watt increased with increasing age (-groups), Watt/kg body weight stayed almost the same in all age-groups. Nevertheless, Watt absolute and Watt/kg body weight (the latter showing an exception with Pre PWV and AIx values) demonstrated to be positively correlated with Pre, Post and ΔPWV as well as Pre AIx values. This indicates that a higher physical performance capacity is accompanied by higher local as well as systemic arterial stiffness, either at rest or after a physical exercise to exhaustion or both. Hence, our third hypothesis that alterations in the arterial stiffness are dependent of the physical performance capacity and that the better trained one is the higher the arterial stiffness is, can be confirmed.

As a result, it seems as if higher physical performance capacity due to regular training in healthy, young, male soccer players is accompanied by a higher arterial stiffness at rest. Although in adults, endurance training has demonstrated to decrease arterial stiffness, in children and adolescents, it might be different due to a critical period of growth and physiological changes in the cause of puberty. Moreover, a higher ΔPWV could mean a higher adaptability of the central arteries and therefore constitute a parameter for an enhanced physical performance capacity. Independently of whether this is the result of, or the requirement for regular training and higher physical performance, this study has demonstrated an acute influence of physical activity to exhaustion on the mechanical properties of arteries in young, trained, male soccer players.

In order to confirm our results and to gain more knowledge regarding different populations, future studies with similar designs should be done for example in endurance trained children and adolescents on the one hand and sedentary or physically inactive children and adolescents on the other hand.

6. Limitations

The following limitations have to be kept in mind concerning this study.

Although, a number of different devices for the measurement of arterial stiffness parameters exist, to our knowledge no one is particularly made for immediate post physical exercise measurements. Neither is the Arteriograph (Tensiomed, Budapest, Hungary; Software Arteriograph 3.0.0.1 for Windows 7), which we used in this study, which resulted in occasional arterial stiffness Post measurements difficulties. In fact, some Post values had to be measured manually out of the gained data, as the software and/or the device was not able to calculate these.

Therefore, a limitation of this study is the use of a device which was not made to gain arterial stiffness data directly after a physical exercise.

Moreover, as our device needs approximately 3 minutes for the measurement, the gained arterial stiffness parameter values do not represent the condition at the maximal effort. For future investigations on the acute effects of physical exercise on arterial stiffness, manufactures of arterial stiffness devices should focus on devices which will allow this kind of measurement. Only if we can investigate influences of physical exercises and loads on the arterial stiffness, during as well as directly after such a physical load, we will be able to gain new knowledge concerning acute as well as chronic adaptations and therefore better understand the complex functions and mechanisms affecting the cardiovascular system.

Another noteworthy limitation has to be pointed out regarding the type of performance load in our athletes. Although a high aerobic capacity is required in soccer athletes, soccer is a game-sport and not an endurance sport per se.

7. List of Figures

8. List of tables

9. References

9.1. Journal Articles

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9.2. Internet

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10. Appendix

10.1. Abbreviations

AIx	Augmentation Index
AIx Pre	Augmentation Index at Rest
AIx Post	Augmentation Index after Ergometry to Exhaustion
AIxao	Aortic Augmentation Index
ANOVA	Analysis of Variance
AP	Augmentation Pressure
AS	Arterial Stiffness
BMI	Body Mass Index
baPWV	Brachial (Ankle) Pulse Wave Velocity
CI	Confidence Interval
cPWV	Central Pulse Wave Velocity
DBP	Diastolic Blood Pressure
ET-1	Endothelin-1
ECG	Electrocardiogram
Hg	Mercury (Element)
HR	Heart Rate
HR_{peak}	Peak of Heart Rate
HR Pre	Heart Rate at Rest
HR Post	Heart Rate after Ergometry to Exhaustion
HR_{max}	Maximal Heart Rate
HRR	Heart Rate Recovery
ISH	Isolated Systolic Hypertension
MAP	Mean Arterial Pressure
NO	Nitrite Oxide/ Nitrogen monoxide
PP	Pulse Pressure
PWV	Pulse Wave Velocity
PWV Pre	Pulse Wave Velocity at Rest
PWV Post	Pulse Wave Velocity after Ergometry
PWVao	Aortic Pulse Wave Velocity
RR	Risk Ratio
SBP	Systolic Blood Pressure
SBPao	Aortic Systolic Blood Pressure
SD	Standard Deviation

VO_2	Oxygen Consumption
VO_{2max}	Maximal Oxygen Consumption
VO_{2peak}	Peak of Oxygen Consumption
WHO	World Health Organisation
ΔPWV	Difference in Pulse Wave Velocity
ΔPWVao	Difference in Aortic Pulse Wave Velocity
ΔAIx	Difference in Augmentation Index
ΔAIxao	Difference in Aortic Augmentation Index
ΔP	Difference in Pressure
ΔV	Difference in Volume

10.2. BMI Reference values of the WHO

"BMI-for-age in Boys, 5 to 19 years z-scores" of the World Health Organisation (WHO) (**http://www.who.int/growthref/who2007_bmi_for_age/en/** ; z-scores: boys, pdf; access on the 21.05.2014).

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
5: 1	61	12.1	13.0	14.1	15.3	16.6	18.3	20.2
5: 2	62	12.1	13.0	14.1	15.3	16.6	18.3	20.2
5: 3	63	12.1	13.0	14.1	15.3	16.7	18.3	20.2
5: 4	64	12.1	13.0	14.1	15.3	16.7	18.3	20.3
5: 5	65	12.1	13.0	14.1	15.3	16.7	18.3	20.3
5: 6	66	12.1	13.0	14.1	15.3	16.7	18.4	20.4
5: 7	67	12.1	13.0	14.1	15.3	16.7	18.4	20.4
5: 8	68	12.1	13.0	14.1	15.3	16.7	18.4	20.5
5: 9	69	12.1	13.0	14.1	15.3	16.7	18.4	20.5
5: 10	70	12.1	13.0	14.1	15.3	16.7	18.5	20.6
5: 11	71	12.1	13.0	14.1	15.3	16.7	18.5	20.6
6: 0	72	12.1	13.0	14.1	15.3	16.8	18.5	20.7
6: 1	73	12.1	13.0	14.1	15.3	16.8	18.6	20.8
6: 2	74	12.2	13.1	14.1	15.3	16.8	18.6	20.8
6: 3	75	12.2	13.1	14.1	15.3	16.8	18.6	20.9
6: 4	76	12.2	13.1	14.1	15.4	16.8	18.7	21.0
6: 5	77	12.2	13.1	14.1	15.4	16.9	18.7	21.0
6: 6	78	12.2	13.1	14.1	15.4	16.9	18.7	21.1
6: 7	79	12.2	13.1	14.1	15.4	16.9	18.8	21.2
6: 8	80	12.2	13.1	14.2	15.4	16.9	18.8	21.3
6: 9	81	12.2	13.1	14.2	15.4	17.0	18.9	21.3
6: 10	82	12.2	13.1	14.2	15.4	17.0	18.9	21.4
6: 11	83	12.2	13.1	14.2	15.5	17.0	19.0	21.5
7: 0	84	12.3	13.1	14.2	15.5	17.0	19.0	21.6
7: 1	85	12.3	13.2	14.2	15.5	17.1	19.1	21.7
7: 2	86	12.3	13.2	14.2	15.5	17.1	19.1	21.8
7: 3	87	12.3	13.2	14.3	15.5	17.1	19.2	21.9
7: 4	88	12.3	13.2	14.3	15.6	17.2	19.2	22.0
7: 5	89	12.3	13.2	14.3	15.6	17.2	19.3	22.0
7: 6	90	12.3	13.2	14.3	15.6	17.2	19.3	22.1

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
7: 7	91	12.3	13.2	14.3	15.6	17.3	19.4	22.2
7: 8	92	12.3	13.2	14.3	15.6	17.3	19.4	22.4
7: 9	93	12.4	13.3	14.3	15.7	17.3	19.5	22.5
7: 10	94	12.4	13.3	14.4	15.7	17.4	19.6	22.6
7: 11	95	12.4	13.3	14.4	15.7	17.4	19.6	22.7
8: 0	96	12.4	13.3	14.4	15.7	17.4	19.7	22.8
8: 1	97	12.4	13.3	14.4	15.8	17.5	19.7	22.9
8: 2	98	12.4	13.3	14.4	15.8	17.5	19.8	23.0
8: 3	99	12.4	13.3	14.4	15.8	17.5	19.9	23.1
8: 4	100	12.4	13.4	14.5	15.8	17.6	19.9	23.3
8: 5	101	12.5	13.4	14.5	15.9	17.6	20.0	23.4
8: 6	102	12.5	13.4	14.5	15.9	17.7	20.1	23.5
8: 7	103	12.5	13.4	14.5	15.9	17.7	20.1	23.6
8: 8	104	12.5	13.4	14.5	15.9	17.7	20.2	23.8
8: 9	105	12.5	13.4	14.6	16.0	17.8	20.3	23.9
8: 10	106	12.5	13.5	14.6	16.0	17.8	20.3	24.0
8: 11	107	12.5	13.5	14.6	16.0	17.9	20.4	24.2
9: 0	108	12.6	13.5	14.6	16.0	17.9	20.5	24.3
9: 1	109	12.6	13.5	14.6	16.1	18.0	20.5	24.4
9: 2	110	12.6	13.5	14.7	16.1	18.0	20.6	24.6
9: 3	111	12.6	13.5	14.7	16.1	18.0	20.7	24.7
9: 4	112	12.6	13.6	14.7	16.2	18.1	20.8	24.9
9: 5	113	12.6	13.6	14.7	16.2	18.1	20.8	25.0
9: 6	114	12.7	13.6	14.8	16.2	18.2	20.9	25.1
9: 7	115	12.7	13.6	14.8	16.3	18.2	21.0	25.3
9: 8	116	12.7	13.6	14.8	16.3	18.3	21.1	25.5
9: 9	117	12.7	13.7	14.8	16.3	18.3	21.2	25.6
9: 10	118	12.7	13.7	14.9	16.4	18.4	21.2	25.8
9: 11	119	12.8	13.7	14.9	16.4	18.4	21.3	25.9
10: 0	120	12.8	13.7	14.9	16.4	18.5	21.4	26.1

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
10: 1	121	12.8	13.8	15.0	16.5	18.5	21.5	26.2
10: 2	122	12.8	13.8	15.0	16.5	18.6	21.6	26.4
10: 3	123	12.8	13.8	15.0	16.6	18.6	21.7	26.6
10: 4	124	12.9	13.8	15.0	16.6	18.7	21.7	26.7
10: 5	125	12.9	13.9	15.1	16.6	18.8	21.8	26.9
10: 6	126	12.9	13.9	15.1	16.7	18.8	21.9	27.0
10: 7	127	12.9	13.9	15.1	16.7	18.9	22.0	27.2
10: 8	128	13.0	13.9	15.2	16.8	18.9	22.1	27.4
10: 9	129	13.0	14.0	15.2	16.8	19.0	22.2	27.5
10: 10	130	13.0	14.0	15.2	16.9	19.0	22.3	27.7
10: 11	131	13.0	14.0	15.3	16.9	19.1	22.4	27.9
11: 0	132	13.1	14.1	15.3	16.9	19.2	22.5	28.0
11: 1	133	13.1	14.1	15.3	17.0	19.2	22.5	28.2
11: 2	134	13.1	14.1	15.4	17.0	19.3	22.6	28.4
11: 3	135	13.1	14.1	15.4	17.1	19.3	22.7	28.5
11: 4	136	13.2	14.2	15.5	17.1	19.4	22.8	28.7
11: 5	137	13.2	14.2	15.5	17.2	19.5	22.9	28.8
11: 6	138	13.2	14.2	15.5	17.2	19.5	23.0	29.0
11: 7	139	13.2	14.3	15.6	17.3	19.6	23.1	29.2
11: 8	140	13.3	14.3	15.6	17.3	19.7	23.2	29.3
11: 9	141	13.3	14.3	15.7	17.4	19.7	23.3	29.5
11: 10	142	13.3	14.4	15.7	17.4	19.8	23.4	29.6
11: 11	143	13.4	14.4	15.7	17.5	19.9	23.5	29.8
12: 0	144	13.4	14.5	15.8	17.5	19.9	23.6	30.0
12: 1	145	13.4	14.5	15.8	17.6	20.0	23.7	30.1
12: 2	146	13.5	14.5	15.9	17.6	20.1	23.8	30.3
12: 3	147	13.5	14.6	15.9	17.7	20.2	23.9	30.4
12: 4	148	13.5	14.6	16.0	17.8	20.2	24.0	30.6
12: 5	149	13.6	14.6	16.0	17.8	20.3	24.1	30.7
12: 6	150	13.6	14.7	16.1	17.9	20.4	24.2	30.9

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
7: 7	91	12.3	13.2	14.3	15.6	17.3	19.4	22.2
7: 8	92	12.3	13.2	14.3	15.6	17.3	19.4	22.4
7: 9	93	12.4	13.3	14.3	15.7	17.3	19.5	22.5
7: 10	94	12.4	13.3	14.4	15.7	17.4	19.6	22.6
7: 11	95	12.4	13.3	14.4	15.7	17.4	19.6	22.7
8: 0	96	12.4	13.3	14.4	15.7	17.4	19.7	22.8
8: 1	97	12.4	13.3	14.4	15.8	17.5	19.7	22.9
8: 2	98	12.4	13.3	14.4	15.8	17.5	19.8	23.0
8: 3	99	12.4	13.3	14.4	15.8	17.5	19.9	23.1
8: 4	100	12.4	13.4	14.5	15.8	17.6	19.9	23.3
8: 5	101	12.5	13.4	14.5	15.9	17.6	20.0	23.4
8: 6	102	12.5	13.4	14.5	15.9	17.7	20.1	23.5
8: 7	103	12.5	13.4	14.5	15.9	17.7	20.1	23.6
8: 8	104	12.5	13.4	14.5	15.9	17.7	20.2	23.8
8: 9	105	12.5	13.4	14.6	16.0	17.8	20.3	23.9
8: 10	106	12.5	13.5	14.6	16.0	17.8	20.3	24.0
8: 11	107	12.5	13.5	14.6	16.0	17.9	20.4	24.2
9: 0	108	12.6	13.5	14.6	16.0	17.9	20.5	24.3
9: 1	109	12.6	13.5	14.6	16.1	18.0	20.5	24.4
9: 2	110	12.6	13.5	14.7	16.1	18.0	20.6	24.6
9: 3	111	12.6	13.5	14.7	16.1	18.0	20.7	24.7
9: 4	112	12.6	13.6	14.7	16.2	18.1	20.8	24.9
9: 5	113	12.6	13.6	14.7	16.2	18.1	20.8	25.0
9: 6	114	12.7	13.6	14.8	16.2	18.2	20.9	25.1
9: 7	115	12.7	13.6	14.8	16.3	18.2	21.0	25.3
9: 8	116	12.7	13.6	14.8	16.3	18.3	21.1	25.5
9: 9	117	12.7	13.7	14.8	16.3	18.3	21.2	25.6
9: 10	118	12.7	13.7	14.9	16.4	18.4	21.2	25.8
9: 11	119	12.8	13.7	14.9	16.4	18.4	21.3	25.9
10: 0	120	12.8	13.7	14.9	16.4	18.5	21.4	26.1

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
10: 1	121	12.8	13.8	15.0	16.5	18.5	21.5	26.2
10: 2	122	12.8	13.8	15.0	16.5	18.6	21.6	26.4
10: 3	123	12.8	13.8	15.0	16.6	18.6	21.7	26.6
10: 4	124	12.9	13.8	15.0	16.6	18.7	21.7	26.7
10: 5	125	12.9	13.9	15.1	16.6	18.8	21.8	26.9
10: 6	126	12.9	13.9	15.1	16.7	18.8	21.9	27.0
10: 7	127	12.9	13.9	15.1	16.7	18.9	22.0	27.2
10: 8	128	13.0	13.9	15.2	16.8	18.9	22.1	27.4
10: 9	129	13.0	14.0	15.2	16.8	19.0	22.2	27.5
10: 10	130	13.0	14.0	15.2	16.9	19.0	22.3	27.7
10: 11	131	13.0	14.0	15.3	16.9	19.1	22.4	27.9
11: 0	132	13.1	14.1	15.3	16.9	19.2	22.5	28.0
11: 1	133	13.1	14.1	15.3	17.0	19.2	22.5	28.2
11: 2	134	13.1	14.1	15.4	17.0	19.3	22.6	28.4
11: 3	135	13.1	14.1	15.4	17.1	19.3	22.7	28.5
11: 4	136	13.2	14.2	15.5	17.1	19.4	22.8	28.7
11: 5	137	13.2	14.2	15.5	17.2	19.5	22.9	28.8
11: 6	138	13.2	14.2	15.5	17.2	19.5	23.0	29.0
11: 7	139	13.2	14.3	15.6	17.3	19.6	23.1	29.2
11: 8	140	13.3	14.3	15.6	17.3	19.7	23.2	29.3
11: 9	141	13.3	14.3	15.7	17.4	19.7	23.3	29.5
11: 10	142	13.3	14.4	15.7	17.4	19.8	23.4	29.6
11: 11	143	13.4	14.4	15.7	17.5	19.9	23.5	29.8
12: 0	144	13.4	14.5	15.8	17.5	19.9	23.6	30.0
12: 1	145	13.4	14.5	15.8	17.6	20.0	23.7	30.1
12: 2	146	13.5	14.5	15.9	17.6	20.1	23.8	30.3
12: 3	147	13.5	14.6	15.9	17.7	20.2	23.9	30.4
12: 4	148	13.5	14.6	16.0	17.8	20.2	24.0	30.6
12: 5	149	13.6	14.6	16.0	17.8	20.3	24.1	30.7
12: 6	150	13.6	14.7	16.1	17.9	20.4	24.2	30.9

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
12: 7	151	13.6	14.7	16.1	17.9	20.4	24.3	31.0
12: 8	152	13.7	14.8	16.2	18.0	20.5	24.4	31.1
12: 9	153	13.7	14.8	16.2	18.0	20.6	24.5	31.3
12: 10	154	13.7	14.8	16.3	18.1	20.7	24.6	31.4
12: 11	155	13.8	14.9	16.3	18.2	20.8	24.7	31.6
13: 0	156	13.8	14.9	16.4	18.2	20.8	24.8	31.7
13: 1	157	13.8	15.0	16.4	18.3	20.9	24.9	31.8
13: 2	158	13.9	15.0	16.5	18.4	21.0	25.0	31.9
13: 3	159	13.9	15.1	16.5	18.4	21.1	25.1	32.1
13: 4	160	14.0	15.1	16.6	18.5	21.1	25.2	32.2
13: 5	161	14.0	15.2	16.6	18.6	21.2	25.2	32.3
13: 6	162	14.0	15.2	16.7	18.6	21.3	25.3	32.4
13: 7	163	14.1	15.2	16.7	18.7	21.4	25.4	32.6
13: 8	164	14.1	15.3	16.8	18.7	21.5	25.5	32.7
13: 9	165	14.1	15.3	16.8	18.8	21.5	25.6	32.8
13: 10	166	14.2	15.4	16.9	18.9	21.6	25.7	32.9
13: 11	167	14.2	15.4	17.0	18.9	21.7	25.8	33.0
14: 0	168	14.3	15.5	17.0	19.0	21.8	25.9	33.1
14: 1	169	14.3	15.5	17.1	19.1	21.8	26.0	33.2
14: 2	170	14.3	15.6	17.1	19.1	21.9	26.1	33.3
14: 3	171	14.4	15.6	17.2	19.2	22.0	26.2	33.4
14: 4	172	14.4	15.7	17.2	19.3	22.1	26.3	33.5
14: 5	173	14.5	15.7	17.3	19.3	22.2	26.4	33.5
14: 6	174	14.5	15.7	17.3	19.4	22.2	26.5	33.6
14: 7	175	14.5	15.8	17.4	19.5	22.3	26.5	33.7
14: 8	176	14.6	15.8	17.4	19.5	22.4	26.6	33.8
14: 9	177	14.6	15.9	17.5	19.6	22.5	26.7	33.9
14: 10	178	14.6	15.9	17.5	19.6	22.5	26.8	33.9
14: 11	179	14.7	16.0	17.6	19.7	22.6	26.9	34.0
15: 0	180	14.7	16.0	17.6	19.8	22.7	27.0	34.1

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
15: 1	181	14.7	16.1	17.7	19.8	22.8	27.1	34.1
15: 2	182	14.8	16.1	17.8	19.9	22.8	27.1	34.2
15: 3	183	14.8	16.1	17.8	20.0	22.9	27.2	34.3
15: 4	184	14.8	16.2	17.9	20.0	23.0	27.3	34.3
15: 5	185	14.9	16.2	17.9	20.1	23.0	27.4	34.4
15: 6	186	14.9	16.3	18.0	20.1	23.1	27.4	34.5
15: 7	187	15.0	16.3	18.0	20.2	23.2	27.5	34.5
15: 8	188	15.0	16.3	18.1	20.3	23.3	27.6	34.6
15: 9	189	15.0	16.4	18.1	20.3	23.3	27.7	34.6
15: 10	190	15.0	16.4	18.2	20.4	23.4	27.7	34.7
15: 11	191	15.1	16.5	18.2	20.4	23.5	27.8	34.7
16: 0	192	15.1	16.5	18.2	20.5	23.5	27.9	34.8
16: 1	193	15.1	16.5	18.3	20.6	23.6	27.9	34.8
16: 2	194	15.2	16.6	18.3	20.6	23.7	28.0	34.8
16: 3	195	15.2	16.6	18.4	20.7	23.7	28.1	34.9
16: 4	196	15.2	16.7	18.4	20.7	23.8	28.1	34.9
16: 5	197	15.3	16.7	18.5	20.8	23.8	28.2	35.0
16: 6	198	15.3	16.7	18.5	20.8	23.9	28.3	35.0
16: 7	199	15.3	16.8	18.6	20.9	24.0	28.3	35.0
16: 8	200	15.3	16.8	18.6	20.9	24.0	28.4	35.1
16: 9	201	15.4	16.8	18.7	21.0	24.1	28.5	35.1
16: 10	202	15.4	16.9	18.7	21.0	24.2	28.5	35.1
16: 11	203	15.4	16.9	18.7	21.1	24.2	28.6	35.2
17: 0	204	15.4	16.9	18.8	21.1	24.3	28.6	35.2
17: 1	205	15.5	17.0	18.8	21.2	24.3	28.7	35.2
17: 2	206	15.5	17.0	18.9	21.2	24.4	28.7	35.2
17: 3	207	15.5	17.0	18.9	21.3	24.4	28.8	35.3
17: 4	208	15.5	17.1	18.9	21.3	24.5	28.9	35.3
17: 5	209	15.6	17.1	19.0	21.4	24.5	28.9	35.3
17: 6	210	15.6	17.1	19.0	21.4	24.6	29.0	35.3

BMI-for-age BOYS
5 to 19 years (z-scores)

World Health Organization

Year: Month	Months	-3 SD	-2 SD	-1 SD	Median	1 SD	2 SD	3 SD
17: 7	211	15.6	17.1	19.1	21.5	24.7	29.0	35.4
17: 8	212	15.6	17.2	19.1	21.5	24.7	29.1	35.4
17: 9	213	15.6	17.2	19.1	21.6	24.8	29.1	35.4
17: 10	214	15.7	17.2	19.2	21.6	24.8	29.2	35.4
17: 11	215	15.7	17.3	19.2	21.7	24.9	29.2	35.4
18: 0	216	15.7	17.3	19.2	21.7	24.9	29.2	35.4
18: 1	217	15.7	17.3	19.3	21.8	25.0	29.3	35.4
18: 2	218	15.7	17.3	19.3	21.8	25.0	29.3	35.5
18: 3	219	15.7	17.4	19.3	21.8	25.1	29.4	35.5
18: 4	220	15.8	17.4	19.4	21.9	25.1	29.4	35.5
18: 5	221	15.8	17.4	19.4	21.9	25.1	29.5	35.5
18: 6	222	15.8	17.4	19.4	22.0	25.2	29.5	35.5
18: 7	223	15.8	17.5	19.5	22.0	25.2	29.5	35.5
18: 8	224	15.8	17.5	19.5	22.0	25.3	29.6	35.5
18: 9	225	15.8	17.5	19.5	22.1	25.3	29.6	35.5
18: 10	226	15.8	17.5	19.6	22.1	25.4	29.6	35.5
18: 11	227	15.8	17.5	19.6	22.2	25.4	29.7	35.5
19: 0	228	15.9	17.6	19.6	22.2	25.4	29.7	35.5

2007 WHO Reference

10.3. Tables of Reference Percentiles for Blood Pressure

Age (years)	Height percentile													
	Boys							Girls						
	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
10														
SBP (mmHg)	108	109	111	112	113	115	116	109	110	111	112	113	115	116
DBP (mmHg)	72	73	74	74	75	75	76	72	73	73	73	73	73	73
Height (cm)	130	133	137	141	146	150	153	130	132	136	141	146	150	153
11														
SBP (mmHg)	110	111	112	114	116	117	118	111	112	113	114	116	118	120
DBP (mmHg)	74	74	75	75	75	76	76	74	74	74	74	74	75	75
Height (cm)	135	137	142	146	151	156	159	136	138	143	148	153	157	160
12														
SBP (mmHg)	113	114	115	117	119	121	122	114	115	116	118	120	122	122
DBP (mmHg)	75	75	75	75	75	76	76	75	75	75	75	76	76	76
Height (cm)	140	143	148	153	158	163	166	143	146	150	155	160	164	166
13														
SBP (mmHg)	115	116	118	121	124	126	126	116	117	119	121	122	123	123
DBP (mmHg)	74	74	74	75	76	77	77	75	75	75	76	76	76	76
Height (cm)	147	150	155	160	166	171	173	148	151	155	159	164	168	170
14														
SBP (mmHg)	119	120	123	126	127	128	129	118	118	120	122	123	123	123
DBP (mmHg)	74	74	75	77	78	79	80	76	76	76	76	77	77	77
Height (cm)	154	157	162	167	173	177	180	151	153	157	161	166	170	172
15														
SBP (mmHg)	123	124	126	128	129	130	130	118	119	121	122	123	123	124
DBP (mmHg)	75	76	78	79	80	81	81	76	76	76	77	77	78	78
Height (cm)	159	162	167	172	177	182	184	152	154	158	162	167	171	173
16														
SBP (mmHg)	126	127	128	129	131	131	132	119	120	122	123	124	124	124
DBP (mmHg)	77	78	79	80	81	82	82	76	76	76	77	78	78	78
Height (cm)	162	165	170	175	180	184	186	152	154	158	163	167	171	173
17														
SBP (mmHg)	128	129	130	131	132	133	134	120	121	123	124	124	125	125
DBP (mmHg)	78	79	80	81	82	82	83	76	76	77	77	78	78	78
Height (cm)	164	166	171	176	181	185	187	152	155	159	163	167	171	174

* Body mass index <85th percentile by 1-year age-sex group (2) according to Centers for Disease Control and Prevention growth charts (3).
† A complete table of the 1st, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 99th percentiles of blood pressure by height percentile in 1-year age-sex groups (Web table 1) is given on the *Journal*'s website (http://aje.oxfordjournals.org/) and at the following website: http://www.geocities.com/bernardrosner/Pediatrics.html.
‡ SBP, systolic blood pressure; DBP, diastolic blood pressure.

List of percentiles by Rosner et al. 2008.

Age, y	Height, cm	SBP, mm Hg					DBP, mm Hg				
		S	50th Percentile (Median)	90th Percentile	95th Percentile	99th Percentile	*S*	50th Percentile (Median)	90th Percentile	95th Percentile	99th Percentile
12	142	0.0762	105	117	120	127	0.1053	65	74	76	81
	145	0.0762	106	117	121	128	0.1053	65	74	76	81
	150	0.0762	107	119	122	129	0.1053	65	74	77	81
	155	0.0762	109	120	123	131	0.1053	66	75	77	82
	161	0.0762	110	121	125	132	0.1053	66	75	77	82
	166	0.0762	111	123	126	133	0.1053	66	75	78	83
	169	0.0762	112	123	127	134	0.1053	67	76	78	83
13	149	0.0780	108	120	123	131	0.1060	66	75	77	82
	152	0.0780	109	121	124	132	0.1060	66	75	78	82
	157	0.0780	110	122	126	133	0.1060	66	75	78	83
	163	0.0780	112	124	127	135	0.1060	67	76	78	83
	169	0.0780	113	125	129	137	0.1060	67	76	79	84
	174	0.0780	114	127	130	138	0.1060	67	77	79	84
	177	0.0780	115	127	131	139	0.1060	68	77	79	84
14	157	0.0799	111	124	128	135	0.1065	67	76	79	84
	160	0.0799	112	125	128	136	0.1065	67	76	79	84
	165	0.0799	113	126	130	138	0.1065	68	77	79	84
	170	0.0799	115	128	132	140	0.1065	68	77	80	85
	176	0.0799	116	129	133	141	0.1065	68	78	80	85
	181	0.0799	118	131	135	143	0.1065	69	78	81	86
	184	0.0799	118	131	135	144	0.1065	69	78	81	86
15	163	0.0819	115	128	132	140	0.1069	68	78	80	85
	165	0.0819	115	128	132	141	0.1069	68	78	80	85
	170	0.0819	117	130	134	142	0.1069	69	78	81	86
	175	0.0819	118	131	135	144	0.1069	69	79	81	86
	180	0.0819	119	133	137	146	0.1069	69	79	82	87
	185	0.0819	120	134	138	147	0.1069	70	79	82	87
	187	0.0819	121	135	139	148	0.1069	70	80	82	87
16	166	0.0839	117	131	135	144	0.1072	69	79	82	87
	169	0.0839	118	132	136	145	0.1072	70	79	82	87
	173	0.0839	119	133	137	146	0.1072	70	80	82	87
	178	0.0839	120	134	139	148	0.1072	70	80	83	88
	182	0.0839	122	136	140	149	0.1072	71	80	83	88
	186	0.0839	123	137	142	151	0.1072	71	81	84	89
	189	0.0839	124	138	142	152	0.1072	71	81	84	89
17	167	0.0860	119	134	138	147	0.1074	71	80	83	88
	170	0.0860	120	135	139	148	0.1074	71	81	83	89
	174	0.0860	121	136	141	150	0.1074	71	81	84	89
	179	0.0860	123	137	142	151	0.1074	72	81	84	90
	183	0.0860	124	139	144	153	0.1074	72	82	85	90
	187	0.0860	125	140	145	154	0.1074	72	82	85	90
	189	0.0860	126	141	146	155	0.1074	72	82	85	91

Height in centimeters for each age represents the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentile. The height percentiles are derived from the overall KiGGS population[18] and are representative for Germany 2003–2006.

BP percentiles apply exactly for the midpoint of each age group (eg, 3 years 6 months old) and can be applied to all children of that age.

LMS skewness parameter $L = -0.4685$ for SBP and $L = 1$ for DBP.

List of percentiles by Neuhauser et al. 2011.

10.4. Zusammenfassung

Parameter der arteriellen Gefäßsteifigkeit, wie die Pulswellengeschwindigkeit (PWV) und der Augmentationsindex (AIx), geben Aufschluss über die Steifigkeit der Arterien und fungieren als unabhängige Prädiktoren für kardiovaskuläre Erkrankungen, Morbidität sowie Mortalität. Während die PWV Auskunft gibt über lokale Zustände des Arterienbaumes, spiegelt der AIx den systemischen Zustand wieder. Beide Parameter werden von extrinsischen wie intrinsischen Faktoren unterschiedlich beeinflusst und ersetzen sich gegenseitig nicht. Studien, welche sich mit den Auswirkungen von sportlicher Aktivität, akut wie chronisch, auf die arterielle Gefäßsteifigkeit beschäftigt haben, zeigen kein homogenes Bild und hinsichtlich dem Kinder- und Jugendalter eine wissenschaftliche Lücke auf.

Ziel dieser Studie war es daher, neben der Erhebung von Ruhewerten der PWV und des AIx, die akuten Auswirkungen einer Ausbelastung auf einem Fahrradergometer auf die Steifigkeit der zentralen Arterien bei jungen (8 - 18 Jahre), gesunden, männlichen Fußballspielern eines österreichischen Profivereins zu untersuchen. Darüber hinaus sollte herausgefunden werden ob es diesbezüglich Unterschiede in Abhängigkeit des Alters gibt und ob Zusammenhänge zwischen der aeroben, körperlichen Leistungsfähigkeit und der arteriellen Gefäßsteifigkeit in diesem Kollektiv bestehen.

PWV Werte in Ruhe lagen über den existierenden Referenzwerten für diese Altersgruppe. Weiters zeigte sich, dass die körperliche Leistungsfähigkeit der untersuchten Fußballspieler über der von gesunden, nicht-sportlichen Vergleichspersonen lag. Im Mittel zeigten die Nachbelastungswerte der PWV eine 84 prozentige Erhöhung gegenüber den Ruhewerten. Darüber hinaus konnte eine Zunahme der PWV, sowohl in Ruhe als auch nach der Belastung, mit zunehmendem Alter beobachtet werden. Die Differenz zwischen den Ruhe- und Nachbelastungswerten (ΔPWV) steigerte sich ebenfalls mit zunehmendem Alter. Der AIx zeigte, im Gegensatz zu anderen Studien, eine negative Korrelation mit dem Alter ($p<0.001$; $\rho=-0.494$), sowie negative Korrelationen mit den Ruhe- ($p<0.001$; $\rho=-0.292$) und Nachbelastungswerten ($p<0.001$; $\rho=-0.367$) der PWV. Watt absolut, sowie Watt/kg Körpergewicht, als Parameter der körperlichen Leistungsfähigkeit, zeigten positive Korrelationen mit den Ruhewerten (absolut: $p<0.001$; $\rho=-0.470$, relativ: n.s.) sowie mit dem Δ der PWV (absolut: $p<0.001$; $\rho=-0.447$, relativ: $p<0.05$; $\rho=-0.225$). Die Tatsache, dass die ΔPWV Werte ebenfalls mit den Nachbelastungswerten positiv korrelierten ($p<0.001$; $\rho=0.948$) zeigt, dass letztere ein großes Δ der PWV bedingen.

Dies legt den Schluss nahe, dass eine gesteigerte körperliche Leistungsfähigkeit bei gesunden männlichen Fußballspielern im Kinder- und Jugendalter, auf Grund regelmäßigen Trainings, mit einer erhöhten arteriellen Gefäßsteifigkeit in Ruhe einhergeht. Wenngleich Studien gezeigt haben, dass Ausdauertraining bei Erwachsenen den gegenteiligen Effekt hat, könnte es sich bei Kindern und Jugendlichen auf Grund physiologischer Veränderungen im Verlauf der Pubertät anders verhalten. Des Weiteren könnte ein großes Δ der PWV im Sinne einer großen Adaptabilität der zentralen Arterien und der Aorta eine Kenngröße gesteigerter körperlicher Leistungsfähigkeit sein. Unabhängig ob als Reaktion auf den Reiz oder als Voraussetzung, zeigen diese Ergebnisse die akute Beeinflussung der mechanischen Eigenschaften des arteriellen Gefäßbaumes auf Grund einer körperlichen Ausbelastung in trainierten Kindern und Jugendlichen.

10.5. Abstract

Arterial stiffness parameters like pulse wave velocity (PWV) and augmentation index (AIx) reflect the mechanical properties of the arteries and constitute independent predictors for cardiovascular diseases, mortality and morbidity. In contrast to PWV, which mirrors local conditions of the arterial tree, AIx reflects the systemic arterial stiffness. Both are differently influenced by extrinsic and intrinsic factors and cannot be used interchangeably. Studies regarding the acute as well as chronic effects of physical exercise on arterial stiffness demonstrate different results and, concerning children and adolescents, are scarce.

Therefore the aim of this study was to ascertain PWV and AIx values at rest (Pre) as well as following a cycle ergometer stress test to exhaustion (Post) in young (8 – 18 years), healthy, male soccer players of an Austrian soccer club. Furthermore, we wanted to find out about influences of age on these parameters and possible correlations between the physical performance capacity and arterial stiffness.

PWV values at rest but also values of the physical performance capacity of the soccer players were increased in contrast to reference values of healthy non-athletes of that age. On average, Post values increases by 84 percent due to the stress test. Furthermore, Pre as well as Post values demonstrated to increase with increasing age. Similar results were found for the difference between Pre and Post values in PWV (∆PWV). In contrast to other studies, AIx showed to be negatively correlated with age ($p<0.001$; $\rho=-0.494$). Negative correlations of AIx were also found with Pre ($p<0.001$; $\rho=-0.292$) and Post ($p<0.001$; $\rho=-0.367$) PWV values. Parameters of the physical performance capacity (Watt absolute, Watt/kg body weight) were positively correlate with Pre (Watt absolute: $p<0.001$; $\rho=-0.470$, Watt/kg: n.s.) as well as ∆PWV values (Watt absolute: $p<0.001$; $\rho=-0.447$, Watt/kg: $p<0.05$; $\rho=-0.225$). As ∆PWV also correlated with Post values of PWV it seems as if a large ∆ is mainly the result of Post PWV values.

In conclusion, it seems as if higher physical performance capacity due to regular training in healthy, young, male soccer players is accompanied by a higher arterial stiffness at rest. Although in adults, endurance training has demonstrated to decrease arterial stiffness, in children and adolescents, it might be different due to a critical period of growth and physiological changes in the cause of puberty. Moreover, a higher ∆PWV could mean a higher adaptability of the central arteries and therefore constitute a parameter for an enhanced physical performance capacity. Independently of whether this is the result of, or the requirement for regular training and higher physical performance, this study has demonstrated an acute influence of physical

activity to exhaustion on the mechanical properties of arteries in young, trained, male soccer players.

11. Declaration

Ich bestätige, dass ich die vorliegende Dissertation selbstständig verfasst, andere als die angegebenen Quellen und Hilfsmittel nicht benutzt und mich auch sonst keiner unerlaubten Hilfe bedient habe, sowie dass ich diese Dissertation bisher weder im In- noch im Ausland in irgendeiner Form als Prüfungsarbeit vorgelegt habe.

12. Curriculum Vitae

Ausbildung:

1988 - 1992	Volksschule in 1020 Wien, Leopoldsgasse
1992 - 2001	AHS – BG9 Wasagasse 10 – Realgymnasium Schulabschluss Matura
10/2001 - 05/2002	Leisten des Präsenzdiensts am Fliegerhorst Brunowski in Langenlebarn
SS 2002 - SS 2007	Studium an der Universität Wien: Bakkalaureatsstudium Gesundheitssport Sportwissenschaften, Abschluss: Bakk.rer.nat. Bakkalaureatsarbeiten: „Ausgewählte Aspekte des Himalayabergsteigens im 20. Jahrhundert.“ im Arbeitsbereich Geschichte des Sports und „Klettersteig-Grundlagen – Auswahl Raxalpe“ in der Abteilung Bewegungswissenschaft und Sportinformatik
SS 2007 - SS 2009	Studium an der Universität Wien: Magisterstudium Sport- und Bewegungswissenschaften
SS 2009	Abschluss des Magisterstudiums Sport- und Bewegungswissenschaften in der Abteilung Sport- und Leistungsphysiologie und den Arbeitsbereichen Trainingswissenschaften und Leistungsphysiologie, Abschluss: Mag.rer.nat. (mit ausgezeichnetem Erfolg) Magisterarbeit: „Arterielle Steifigkeit, Blutdruck und körperliche Aktivität – Zusammenhänge, Funktionen und Wirkungsweisen“.
Seit SS 2009	Dissertationsstudium der Sportwissenschaften in der Abteilung Sport- und Leistungsphysiologie und den Arbeitsbereichen Trainingswissenschaften und Leistungsphysiologie. Themabereiche und Arbeitsfelder der Arbeit: Arterial Aging, Blood Pressure, Cardiovascular System and Physical Exercise, Growth Factors
WS 2006/07 - SS 2012	Studium an der Universität Wien: Diplomstudium Biologie
SS 2012	Abschluss des Diplomstudiums Biologie in der Abteilung Neurobiologie, Abschluss: Mag.rer.nat. (mit ausgezeichnetem Erfolg)

Diplomarbeit: „The spider *Heteropoda venatoria* and its visual system“.

Stipendien

2009	Leistungsstipendium der Universität Wien
2010	Leistungsstipendium der Universität Wien

Wissenschaftliche Erfahrungen

Beiträge

02.- 05.07.2014	Oral presentation at the “19th annual Congress of the European College of Sports Science”, Amsterdam, Netherlands

Wissenschaftliche Kongressbesuche:

04.- 05.12.2009	“Präventionstage Wien 2009”, Wien
15.- 17.04.2010	“6th International Symposim on Arterial Stiffness”, Pecs, Hungary
26.- 28.09.2012	„14. Kongress der Österreichischen Sportwissenschaftlichen Gesellschaft (ÖSG)“, Salzburg
18.- 20.10.2012	„Artery12“, Wien
09.- 11.11.2012	„Berg und Sport 2012”, Ramsau am Dachstein
09.04.2013	1st Scientific Meeting on „Active Ageing“, Wien
02.- 05.07.2014	“19th annual Congress of the European College of Sports Science”, Amsterdam, Netherlands

Wissenschaftlicher Buchbeitrag:

„Molekulare Sport- und Leistungsphysiologie“; Norbert BACHL, Herbert LÖLLGEN, Harald TSCHAN, Henning WACKERHAGE, Barbara WESSNER (Hrsg.)
Co-Autor in den Kapiteln:
„Wachstumsfaktoren unter besondere Berücksichtigung des muskuloskelettaren Systems“, „Herzkreislaufsystem“, „Bindegewebe“
http://www.springer.com/medicine/book/978-3-7091-1590-9

Wissenschaftliche/Universitäre Lehrtätigkeit:

SS 2012 - SS 2014	Am Zentrum für Sportwissenschaften und Universitätssport (ZSU), Universität Wien, Proseminar „Einführung in das wissenschaftliche Arbeiten“
WS 2012 – WS 2013	Am ZSU, Basismodul „Studienorientierung“
Im SS 2010	Tutor in den Tierphysiologischen Übungen – Neurologie
Im SS 2011	Lehrauftrag in den Tierphysiologischen Übungen – Neurologie

Berufliche Erfahrung:

06/2003	Ferialpraktikum am Internationalen Flughafen Wien Schwechat
2006	Praktikum im Kurzentrum Oberlaa
2008	Praktikum am Institut für Medizinische und Sportwissenschaftliche Beratung (IMSB) Wien.
2005-2011	Geringfügige Anstellung bei dem Bergsportfachgeschäft „Bergfuchs GmbH“ in Wien.
11.2011 – 04.2014	Angestellt als PraeDoc / Universitätsassistent an der Universität Wien, Zentrum für Sportwissenschaften und Universitätssport in der Abteilung für Sport- und Leistungsphysiologie.

Berufliche Zusatzausbildungen:

2013	Ausbildung zum lizensierter Kettlebell Instructor
2013	Ausbildung zum lizensierter Spinning Instructor
2005	Schulung zur Untersuchungsdurchführung an den Geräten „MediMouse“ und „Dr. Wolff Back.Check“
2004	Ausbildung zum lizensierter Snowboardlehrer