The creation of an arterial anatomy reference data set for a South African population

by

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Abstract

Arterial pathology is one of the main contributors to cardiovascular diseases and mortality. Several studies have been done to investigate the association between changes in arterial dimensions and cardiovascular risk factors.

During the process of ageing, the structural and functional properties and capabilities of arteries are altered. The arterial lumen increases with age and thus the arterial diameter could be used as an indicator for the overall ageing process. Researchers have reported sexual dimorphism in arterial dimensions for several arteries. Body size may confound the effect of sex on arterial dimensions because vascular surgery may be more difficult in smaller patients who may have proportionally smaller arteries. Smaller patients are likely to have shorter necks, which may limit surgical access to the carotid arteries. The question arises whether sex or body size contribute more to dimensional changes.

The aim of this study was to evaluate the influence of specific parameters (age, weight, height, body mass index and sex) on the variations in arterial anatomy in a South African population. A primary reference data set was compiled regarding these variations for a cadaver population. This primary reference data set will serve as the first step to a greater database of arterial measurements that could be sorted according to the above-mentioned parameters. To determine whether the results were an accurate reflection, a secondary data set was compiled for a living population and compared with the results from the cadaver population, specifically for the parameters age and sex.

For the South African population studied, smaller arteries were found in females and no statistical significant difference was observed between the elastic arteries and the muscular arteries. Only the coronary arteries showed a statistical significant difference between the left and right side. The left coronary artery had a larger outer and inner diameter as compared to the right coronary artery. The results showed no statistical significance between the cadaver and living population, the left common

carotid – and left subclavian arteries being the exceptions. Arterial size increased with an increase in body size and age.

Data on normal arterial dimensions for a South African population is scarce, but essential when evaluating whether a dilatation or stenosis are pathological. Knowledge of the normal arterial dimensions at a specific arterial site can contribute to early diagnosis and successful intervention for a variety of cardiovascular conditions.

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Abdominal aorta at level of celiac trunk	(AC)
Abdominal aorta before terminal bifurcation	(AB)
Ascending aorta superior to fibrous pericardium	(AA)
Body mass index	(BMI)
Coronary artery disease	(CAD)
Computed tomography	(CT)
Digital Imaging and Communications in Medicine	(DICOM)
Female	(F)
Inner diameter	(ID)
Left	(L)
Left brachial artery before bifurcation	(LBA)
Left common carotid artery at origin	(LCC)
Left common iliac artery at origin	(LCI)
Left coronary artery at origin	(LCA)
Left femoral artery at origin	(LFA)
Left internal carotid artery distal to carotid body	(LIC)
Left popliteal artery in popliteal fossa	(LPA)
Left subclavian artery at origin	(LSC)
Male	(M)
Magnetic resonance imaging	(MRI)
Outer diameter	(OD)
Peripheral arterial disease	(PAD)
Right	(R)
Right brachial artery before bifurcation	(RBA)
Right common carotid artery at origin	(RCC)
Right common iliac artery at origin	(RCI)
Right coronary artery at origin	(RCA)
Right femoral artery at origin	(RFA)
Right internal carotid artery distal to carotid body	(RIC)
Right popliteal artery in popliteal fossa	(RPA)
Right subclavian artery at origin	(RSC)
South African Demographic and Health Survey	(SADHS)
Standard deviation	(SD)
Trans-catheter heart valve	(THV)
United States of America	(USA)
Wall thickness	(WT)

1. Introduction

1.1 The importance of clinical anatomy and cadaveric research

A thorough understanding of the anatomy of the human body forms a fundamental part of medical practice. [1] Demonstrating an advanced knowledge of arterial anatomy, when tending to cardiovascular patients, can eliminate possible complications and accelerate the diagnosis to the benefit of the patient. Clinical anatomy therefore remains one of the most valuable subjects to any medical practitioner. [2,3]

For centuries, the use of cadavers to teach clinical anatomy has been of key importance in medical education around the world. Community outlooks, cultural philosophies, ethical unease, unfavourable publicity regarding body donation, the costs of a body donation program and hesitation surrounding the educational value of cadaver dissections have all played a part in severely restricting the access educational institutions have to cadavers. As a result, some educational institutions have totally abandoned the use of cadavers for teaching clinical anatomy. [4-7] However, many have continued their voluntary body donor programs [7,8], and others have reinstated their programs after attempting to abandon or restrict it. [6,7] Educational institutions in New York, Hawaii, California and Washington all found that the standard of the anatomical knowledge displayed by their students was negatively affected by the removal of dissection programs. [6,7] Although it is well accepted that the experience gained from cadaver dissections varies between individual students, the educational value of cadaver dissections covers much more than only anatomical education, especially when considering postgraduate anatomical research. [6,7,9-11]

Anatomical research providing us with the knowledge of normal arterial dimensions at a given anatomical point can contribute to determining the severity of a cardiovascular disease when the normal arterial diameter is compared to a narrowed or dilated arterial diameter. Studies on the relation between changes in arterial dimensions and cardiovascular risk factors have been done in the coronary artery [12],

different aortic segments [13-20], common iliac artery [15,19], common carotid artery [21,22] and internal carotid artery. [21,22] Living populations [13-15,17,19] as well as cadavers [12,16,18] were used in these studies.

Although image diagnostic methodology such as ultrasound, magnetic resonance imaging (MRI) and computed tomography (CT) becomes more accurate every day, cadaver studies remain important for acquiring medical knowledge, particularly studies intending to clarify anatomical-morphological features. [7,9,10,23,24] Limitations of cadaver studies include the possibility that the use of cadaveric tissue may yield measurements that do not accurately reflect a living population. However, arteries contain a high percentage of elastic tissue and smooth muscle in the tunica media, the middle layer of the arterial wall, and therefore arteries are not prone to collapse and should accurately reflect their true diameter. [25] A living-population component is often added to cadaver studies in order to compare the two populations, analyse the comparisons and differences and ultimately conclude whether the use of cadaveric tissue is an accurate reflection of the living population.

1.2 Cardiovascular complications and morphometric arterial variations

An age-related increase exists in the dilatation of the arterial lumen [13-17,19,21,22,26,27] and thus the arterial diameter is a useful indicator of the vascular ageing process. The principle changes that occur with vascular ageing are arterial dilatation, increase in wall thickness and decrease in elasticity and compliance. [26-28] Alterations of large arteries are a major factor of cardiovascular morbidity and mortality. [26] Hypertension, atherosclerosis, diabetes mellitus, hyperlipidaemia, smoking and other risk factors accelerate age-related changes in the structure, function and dimensions of arterial anatomy. These factors contribute to undesirable clinical outcomes related to the arterial system such as arterial aneurysms and arterial dissections (see 1.4.1 & 1.4.2). [17,19,21,22,26,27]

Changes in arterial dimensions are influenced by different processes in adults and children. [27] In children and adolescents, morphological factors and growth are the major contributors, whereas in adults, vascular ageing and cardiovascular risk

factors contribute more. Furthermore, the influence of various factors differs according to the arterial site. [27]

Arterial dimensions are influenced by interrelated pathological and physiological processes. Pathological studies have shown a reduced arterial diameter in the early stages of atherosclerosis, although a compensatory physiological response can cause enlargement in the later stages. [29,30] Cardiovascular diseases lead to physiological responses such as ectasia (dilatation of a tubular structure), increased myocardial demands and high-flow fistulae. These are all conditions that increase arterial diameters. These physiological responses may cause a widespread increase in arterial dimensions that are not limited to a specific arterial segment only. It is therefore difficult to establish whether an arterial segment that appears normal, is truly normal. [30] This causes a problem with regard to the conventional radiographic estimation of the severity of a cardiovascular disease. The percentage of stenosis is a ratio, based on the diameter of a narrowed arterial segment to the diameter of a normal arterial segment of a specific arterial site. [30] Unfortunately, due to the difficulty to accurately assess normal arterial diameter in humans, because of possible physiological responses, the clinical efficacy of this estimate is diminished. The solution to this problem is to find methods whereby normal arterial diameter, at a given anatomical point, may be predicted and used as normal reference to calculate the percentage of stenosis. At present, South African data on the normal diameter of human arteries are not available in a methodical format.

Observations made by several earlier researchers [13-17,20-22,26-33] fuelled the interest to explore and evaluate the influence of variables associated with an increased risk of cardiovascular complications on the morphometric variations in arterial diameters at a variety of arterial sites.

1.3 The influence of cardiovascular complications

1.3.1 Hypertension

Hypertension is a condition characterised by a temporary or persistent increase in systemic blood pressure to a level that will lead to cardiovascular damage or other undesirable clinical outcomes. Hypertension is defined by a systolic blood pressure

above 140 mmHg or a diastolic blood pressure above 90 mmHg. [34] Consequences of uncontrolled hypertension include retinal vascular damage, cerebrovascular disease, stroke, left ventricular hypertrophy, cardiac failure, myocardial infarction, arterial dissection, arterial aneurysm and renovascular disease. [26,27,34] An underlying disease, such as renal disease or pheochromocytoma, is identified as being the cause of hypertension in less than 10% of all cases. The balance, traditionally labelled essential hypertension, arises from a variety of disturbances in the normal pressure-regulating mechanisms of arteries, which negatively influence the cardiovascular system and accelerate age-related changes. [17,19,21,22,26,27,34]

Due to the widespread prevalence and the impact on cardiovascular health, hypertension is a major cause of disease and death in industrialised societies. It is estimated that 24% of people living in the United States of America (USA), including about 50% of all residents over the age of 60 years, have hypertension, but that only about 33% of these people are aware of their condition. It is estimated that people who have normal blood pressure at the age of 55 years still have a 90% lifetime risk of becoming hypertensive, a clear indicator that age plays a significant role in the development of this life-threatening condition. [34]

The treatment of hypertension and its complications in the USA has an estimated cost of $37 billion annually. Hypertension is the primary cause of 35 000 deaths annually in the USA, and is a contributing factor in a further 180 000 deaths. It is associated with a threefold increase in the risk of myocardial infarction and a seven to tenfold increase in the risk of stroke. [34]

The first South African Demographic and Health Survey (SADHS) in 1998 described the national prevalence of hypertension. [35] It was found that 25% of males and 26% of females had blood pressure above 140/90 mmHg and 11% of males and 14% of females had blood pressure above 160/95 mmHg. Of these patients, 41% of males and 67% of females were aware of their condition, 39% of males and 55% of females used antihypertensive medication, and 26% of hypertensive males and 38% of females had their blood pressure controlled below 160/95 mmHg. The poor level of hypertension control in South Africa highlighted the need to identify people at risk

as well as people needing intervention. Early diagnosis and cost-effective control are of key importance in the control of this widespread cardiovascular condition. [35]

Data from the SADHS show that differences in the prevalence of hypertension are not ethnically based and can be accounted for by other socio-economic and socio-demographic parameters. Hypertension is strongly associated with the consumption of excessive amounts of salt, stress, decreased physical activity, and an increased age. Notably, females seem more prone to hypertension, suggesting a sex difference regarding changes in arterial anatomy leading to hypertension. [35]

In 1929, Donnison described blood pressure patterns in a Kenyan community living in “conditions which have probably undergone no appreciable change for many centuries.” [36] Donnison described a similar normal blood pressure pattern found in Europe and Africa for individuals below the age of 40 years. A rise in blood pressure was observed in patients over the age of 40 years in Europe, but no increase was observed in Africa. He contrasted the unchanged patterns of existence for a large number of generations in the Kenyan population, with the revolutionary changes in the living circumstances of the European population and blamed greater mental stress for the hypertension observed in the European population. [36]

Today, more than 85 years later, when change has been sweeping through Africa, extensive epidemiological studies show that hypertension is one of the most common cardiovascular diseases in Africa and that blood pressure sharply increases with an increase in age. This supports the findings of the 1998 SADHS regarding the correlation between hypertension and socio-economic and socio-demographic factors. [35,36] It seems that certain lifestyle factors, accompanied by an increase in age, lead to severe changes in arterial anatomy, resulting in cardiovascular conditions.

The second SADHS in 2003 recorded national blood pressure levels much lower than the levels recorded in 1998, leading to the apparent prevalence rate of hypertension in 2003 being reduced by almost half. This unrealistic and idealistic finding incited a series of investigative processes attempting to find a justification for this phenomenon. This included assessing whether the risk factor profile was

significantly different or whether the use of antihypertensive medication had changed. [37] An unchanged pattern of hypertension risk factors, as well as a similar proportion of participants for whom antihypertensive medication was recorded in 1998 was found after investigative processes in 2003 was concluded, indicating that there were no major shifts in the management of hypertension. [37]

Although the results of the survey were presented in the 2003 official report, caution should be exercised in the interpretation thereof, as it is likely that the data do not reflect the true situation regarding hypertension in South Africa. Furthermore, the proportion of participants with hypertension who were taking drugs, unrealistically increased, as did the proportion with controlled hypertension. [37] No new SADHS has been conducted since 2003.

Hypertension is frequently associated with the presence of structural and dimensional changes in the cardiovascular system, as seen with increased age. [38] The presence of left ventricular hypertrophy, an increased thickness of the carotid arterial wall and a greater wall-to-lumen ratio in small resistance arteries may be extremely important in hypertension, both from a pathophysiological and a clinical prognostic point of view. [38]

Biological factors such as changes in arterial dimensions due to age, socio-economic stress, lack of access to facilities, poor diet, obesity, dietary excess, alcohol consumption and lack of exercise are considered the primary causes of hypertension. [39] Due to the extensive list of lifestyle factors and biological factors contributing to hypertension, both lower-income groups and higher-income groups may be at increased risk for structural and dimensional arterial changes.

1.3.2 Atherosclerosis

At present arteriosclerosis or arterial stiffness is classified into three lesions: atherosclerosis, calcified sclerosis and arteriolosclerosis. [25,41] Atherosclerosis, the most common form of arteriosclerosis, is a complex process that begins with the appearance of cholesterol-laden macrophages in the tunica intima of large and medium sized arteries. This generally leads to narrowing of the arterial lumen and eventually causes fibrosis and calcification of the arterial wall. [40] The clinical

manifestations of atherosclerosis include stable angina and coronary artery disease (CAD). [41] Stable angina is a predictable pattern of chest pain usually associated with activity or stress. [25]

Atherosclerotic plaque has a tendency to accumulate in areas where arteries branch, curve or are irregular, as well as in areas where blood undergoes abrupt changes in velocity and direction of flow. [41]

The original understanding of atherosclerosis is that plaque produce arterial stenosis. The degree of stenosis was thought to be the main factor in diseases such as CAD. It is now believed that after an initial stenosis in the earliest stages, atherosclerotic plaque grow outward, rather than inward for much of the patient's life history, so that substantial atherosclerosis can exist without producing stenosis. Hence, significant atherosclerosis may be silent clinically and invisible on angiograms, as a narrowing will not always be detected. [41]

Diagnosis of atherosclerosis is usually based on patient history and physical examination, and confirmed by imaging techniques. [40] However, due to physiological responses it is difficult to determine with image diagnostic methodology whether a certain arterial segment is narrowed, normal or dilated when only using the conventional radiographic estimation of percentage of stenosis and not having a reference of what is truly normal. [29,30]

The general assumption is that atherosclerosis, as with hypertension, is caused by biological and lifestyle risk factors for example socio-economic stress, lack of access to facilities, poor diet, obesity, dietary excess, alcohol consumption, lack of exercise and increase in age. [42] With the rapid development of the pharmaceutical industry and the increase in life expectancy as seen in the developed world between 1800 and 2000, vascular disease has replaced infectious disease as the primary cause of death across the developed world. [31,32] The general assumption that atherosclerosis is mostly related to lifestyle leads to the understanding that if modern populations could imitate pre-industrial or even pre-agricultural lifestyles, then atherosclerosis, or at least its symptoms, could be avoided. However, atherosclerosis was found to be common in four pre-industrial populations, including a pre-agricultural hunter-

gatherer population, and was found across a wide span of human history. [32] The presence of atherosclerosis in ancient human populations suggests that the disease is not characteristic of any specific diet or lifestyle, but rather related to the morphometric arterial changes associated with ageing. [31-33]

The prevention of atherosclerosis is a major objective of modern medicine. Treatment is largely mechanical: balloon stretching, laser ablation, surgical removal of atherosclerotic plaque, and various grafting and bypass procedures. [40] Having an arterial anatomy reference data set for a South African population can contribute to the determination of graft, stent or balloon size, thus decreasing postoperative complications and increasing success rate.

1.3.3 Diabetes mellitus

Diabetes mellitus is a chronic metabolic disorder where the metabolic use of carbohydrates is impaired and the use of lipid and protein is enhanced. It is caused by an absolute or relative deficiency of insulin and long term complications include generalised degenerative changes in large and small arteries. [43]

Diabetes mellitus increases the likelihood of developing several vascular diseases, falling under the umbrella term of diabetic vascular disease. The risk for developing diabetic vascular disease increases with an increase in age, the presence of hypertension, smoking, lack of physical exercise, obesity, a high-fat diet and being of the male sex. [43,44]

Patients with diabetes mellitus have too much glucose in the bloodstream because of the body's inability to either produce insulin or to use insulin efficiently. [44] Over time, high blood glucose levels damage the arteries, leading to cardiovascular complications, the leading cause of death among people with diabetes mellitus. [44]

Two major types of vascular diseases that diabetic patients often suffer from are CAD and cerebrovascular disease. Diabetic vascular disease refers to diseases that cause the development of blockage in the arteries throughout the body. [43,44] Patients with diabetes mellitus are also at risk of cardiac failure. Narrowing or blockage of the

blood vessels in the legs, a condition called peripheral arterial disease (PAD) also occurs in patients with diabetes mellitus. [44]

CAD, also referred to as ischaemic heart disease, is caused by a hardening or thickening of the walls of the coronary arteries. Cerebrovascular disease affects blood flow to the brain due to the narrowing, blockage, or hardening of the common carotid - and internal carotid arteries. [44]

Diabetic patients are at risk of developing serious health conditions, including blindness, severe kidney disease, stroke, myocardial infarction, or sores on their feet. Eventually, dead tissue develops, which is known as gangrene, that could lead to infection and ultimately to amputation. [44]

If normal arterial dimensions at a given anatomical point can be defined, this knowledge can contribute to quantifying the severity of diabetic vascular disease. Early intervention and diagnosis of diabetic vascular disease is of key importance and as with atherosclerosis, an arterial anatomy reference data set can contribute to the determining the correct graft, stent or balloon size when treating the stenosis caused by diabetic vascular diseases such as CAD or PAD.

1.3.4 Hyperlipidaemia

Hyperlipidaemia refers to elevated levels of lipids in the blood plasma. [45] Excess lipids such as low density cholesterol and triglycerides are deposited in the arterial walls, resulting in arterial narrowing and hardening without any visible symptoms. Symptoms will eventually appear when the clogged arteries supplying vital organs such as the brain and heart are no longer capable of supplying the oxygen and nutrient demands of these organs. Hyperlipidaemia is a precursor of other cardiovascular complications such as CAD, cerebrovascular disease and myocardial infarction. [46]

Two thirds of the world population have total blood cholesterol levels above 5.0 mmol/L. The prevalence of raised cholesterol levels increases with age and is especially prevalent in females. [46] In males, the proportion of the population with cholesterol levels above 5.0 mmol/L increases from 23% in those aged between 16

and 24 years, to 82% in those aged between 55 and 64 years. This compares with 27% of females aged between 16 and 24 years and 91% in those aged between 55 and 64 years. [46]

Influenced by sex and age, hyperlipidaemia is a typical cardiovascular risk factor that accelerates age-related changes in arterial anatomy, leading to the formation of arterial aneurysms and arterial dissections. [17,19,21,22,26,27,45]

1.3.5 Smoking

Cigarette smoking causes 1 out of 5 deaths in the USA annually. It is the main preventable cause of death and illness in the developed world. Smoking harms nearly every organ in the body, including the heart, blood vessels, lungs, eyes, mouth, reproductive organs, bones, bladder, and digestive system. [47]

The chemicals in tobacco smoke harm the blood cells and damage the structure and function of the heart and blood vessels. Smoking causes a loss of distensibility and compliance in arteries, causing an increase in the risk of atherosclerosis, CAD, myocardial infarction and PAD. [47,48]

Smoking is a major cardiovascular risk factor when combined with other risk factors such as hyperlipidaemia, hypertension, obesity and increased age. [47,48] Even light or occasional smoking, damages the cardiovascular system. For women who use birth control pills and diabetic patients, smoking poses an even greater risk of damage to the heart and blood vessels. [47]

The smoke from the burning end of a cigarette, cigar, or pipe (second-hand smoke), can also harm the cardiovascular system. Second-hand smoke also refers to smoke that is breathed out by a person who is smoking and is just as harmful to the heart and the blood vessels of non-smokers as smokers. [47]

Smoking has been directly linked to the increase in growth of arterial dissections and arterial aneurysms. [47] Strachan found smoking to be a major risk factor and predictor of death from an arterial dissection or an arterial aneurysm. [48]

When considering all of these cardiovascular risk factors, it is clear that the inevitable parameters, age and sex, contribute to the development of various cardiovascular diseases.

An increased age, increased BMI, and being of the female sex are considered risk factors for the development of hypertension and eventually leading to stroke and cardiac failure. An increase in age and increase in BMI also contribute to the development of atherosclerosis leading to CAD. Men with an increased age and BMI are predisposed to the development of diabetes mellitus that can cause PAD. Hyperlipidaemia is commonly found in older females and can lead to complications like CAD, cerebrovascular disease and myocardial infarction. The strain these diseases assert on the arterial system can lead to undesirable clinical outcomes such as arterial dissection and arterial aneurysm.

1.4 Undesirable clinical outcomes

Blood is ejected from the left ventricle of the heart into the ascending aorta and aortic arch, which have branches supplying the heart, head and upper extremities. The descending aorta has branches supplying the thorax, abdomen as well as lower extremities. [49]

The aorta plays an important role in the circulation of blood. When the heart contracts, the aorta expands, thus converting kinetic energy from the contracting ventricle to potential energy stored in the aortic wall. Upon recoil, the potential energy stored in the aortic wall is converted back into kinetic energy; blood is forced forward, given that the aortic valve is closed. [49,50]

Large arteries, including the aorta, have three layers: the tunica intima, the tunica media, and the tunica adventitia (Figure 1). The tunica media contains relatively little smooth muscle and large amounts of elastic tissue which is responsible for the important recoil properties of the aorta. [49]

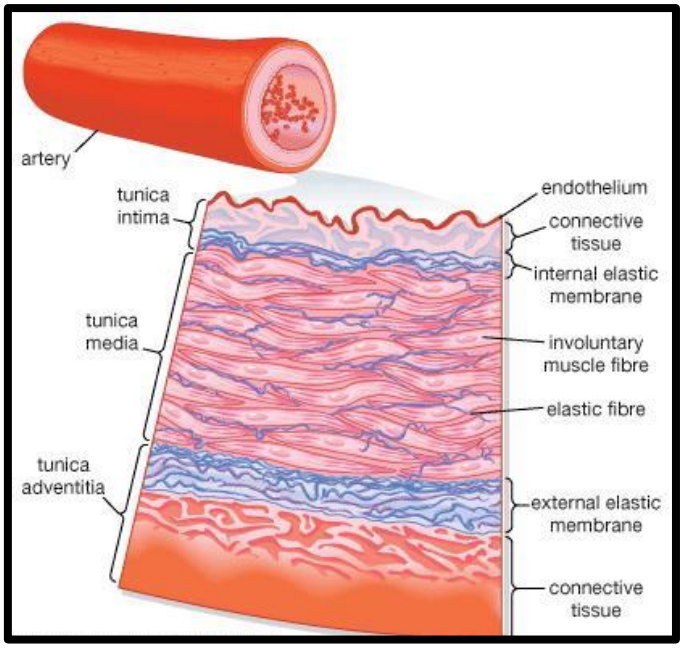

Figure 1: Layers of the arterial wall. [25]

Broad-spectrum arterial diseases and undesirable clinical outcomes can be grouped into arterial dissection and arterial aneurysm. Arterial dissection is defined as a tear in the tunica intima resulting in separation of tissue within the tunica media. Arterial aneurysm is defined as the process where an artery responds to increased stress by atypical dilatation. Since the aorta is the principal artery in the human body, diseases of the aorta could have serious consequences. [49.50]

If changes in arterial dimensions can be accurately assessed, the subsequent early diagnosis of arterial disease can decrease the morbidity and mortality related to these undesirable clinical outcomes.

1.4.1 Arterial dissection

Arterial dissection was officially defined by Morgagni in 1761. He described it as the devastating incident when circulating blood causes a tear that leads to the separation of the layers of the tunica media along various lengths of an artery. [50]

Symptoms vary with the type of arterial dissection and therefore it is important for medical professionals to become familiar with the different classifications based on the distribution of the dissection, specifically along the aorta. [49-53]

Aortic dissection can occur along any portion of the ascending thoracic -, descending thoracic - or abdominal aorta. There are several classification schemes for aortic dissections: the Type A and B Stanford classification system (Figure 2) and the Type I, II and III DeBakey classification system (Figure 3). Aortic dissections are classified into these categories depending on their location and extent. The distinction is important because treatment strategies and prognoses are suggested with regard to location. [49-51,53]

In the proximal Stanford Type A dissection, the ascending thoracic aorta is involved, regardless of the site of the primary tear. In the distal Stanford Type B dissections, neither the ascending thoracic aorta nor the aortic arch is involved and the dissection is confined to the descending thoracic aorta or abdominal aorta. [50] The Stanford classification system is more commonly used in practice with approximately two thirds of dissections being Stanford Type A, and one third being classified as Stanford Type B. [51,52]

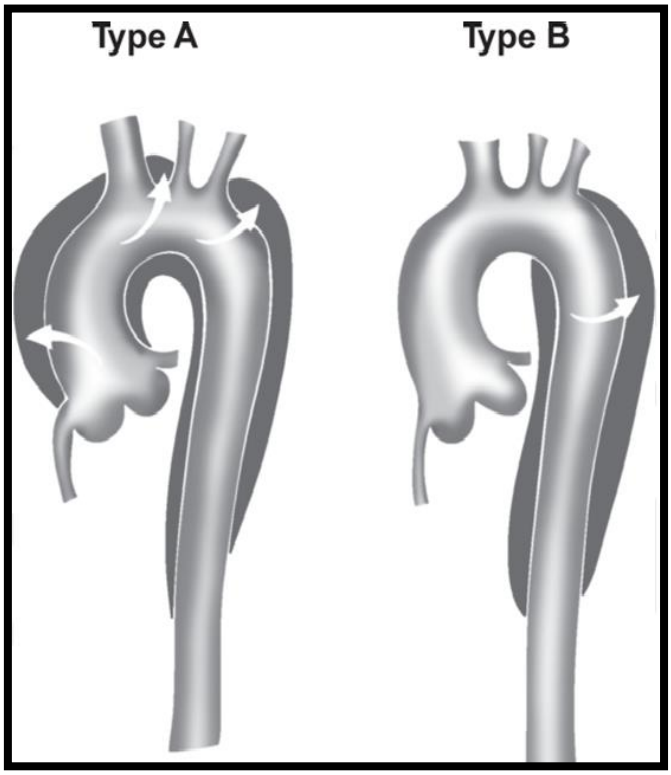

Figure 2: Stanford classification. [52]

The less commonly used anatomical classification introduced by DeBakey includes Type I which involves the ascending aorta as well as the descending aorta, Type II

which is confined to the ascending aorta, and Type III which only involves the descending aorta. [52]

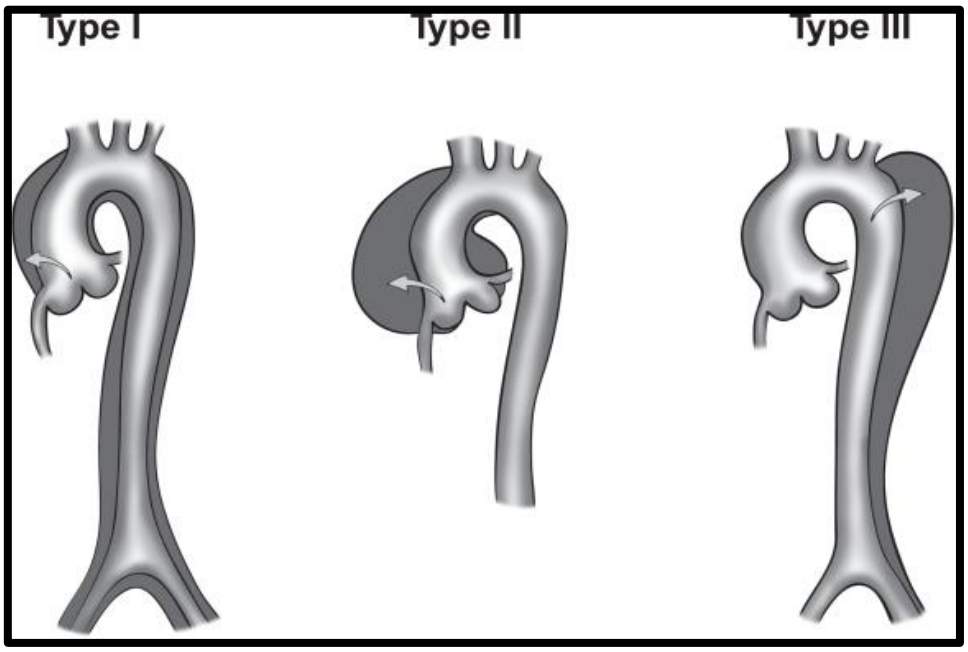

Figure 3: DeBakey classification. [52]

Proximal aortic involvement, Stanford Type A or DeBakey Type I and II, tends to be more devastating because of the potential for extension into the branches of the aortic arch forming carotid dissection, the support structures of the aortic valve, or the pericardial space. [51]

Any degenerative condition that interferes with the normal integrity of the elastic or muscular components of the layers of an artery can predispose to arterial dissection. Degeneration most commonly arises from hypertension, ageing or cystic medial degeneration that is characteristic of hereditary connective tissue disorders, such as Marfan syndrome and Ehlers-Danlos syndrome. [51]

1.4.2 Arterial aneurysm

An arterial aneurysm is generally defined as an artery with a diameter of 1½ times that of the normal artery as suggested by the Society of Vascular Surgery and the International Society for Cardiovascular Surgery. [54] In a clinical setting, a diameter larger than 30 mm in the abdominal aorta was originally considered to be an aneurysm. An abdominal aortic aneurysm was operated on when it exceeded 50-55

mm, due to the risk of rupture. [54] Today, researchers vary in their numerical definitions of an aneurysm. This can be due to the differences in age, sex, body size and ethnicity of the different population groups studied. If normal arterial diameter at a specific arterial site can be determined it can aid in the diagnosis of arterial aneurysms in different individuals by simply using the 1½ times guideline.

Aneurysms are (by definition) limited to a specific area in patients but may in some individuals be multiple. Aneurysms dilate gradually, increasing the risk of rupture. In popliteal aneurysms, thrombosis can develop, increasing the risk of embolisation distally. [54]

The most common location for an aneurysm is in the abdominal aorta with a prevalence of 5-6% in males and 1-2% in females, over the age of 65 years. About 30% of patients with a popliteal artery aneurysm, also have an abdominal aortic aneurysm. However, relatively few patients with an abdominal aortic aneurysm have a popliteal artery aneurysm. [55,56] The incidence of an aneurysm in the coronary artery is 1.5-5%, with a predisposition for the right coronary artery and the prevalence of cerebral aneurysms is about 2%. [57,58] Around 18% of patients with an abdominal aortic aneurysm have coronary artery ectasia or coronary artery aneurysm formation. [59]

Some researchers suggest that the entire vascular tree is abnormal in patients with arterial aneurysmal disease, where abdominal aortic aneuryms have been associated with widespread arteriomegaly, or reduced distensibility at distal arterial sites. [61] Other observations indicate that an abdominal aortic aneurysm is associated with abnormalities in the central, elastic arteries only. [60]

The most common environmental risk factors for arterial aneurysmal disease are age, male sex and smoking. The abdominal aorta appears to be particularly sensitive to smoking. [59] Previously it was thought that an abdominal aortic aneurysm was strongly associated with atherosclerosis, but this relationship is being questioned, because aneurysms are rarely found in locations that are considered to be prone to atherosclerosis such as the femoral or common iliac arteries. [54] Furthermore, diabetes mellitus seems to be a negative risk factor for acquiring an abdominal aortic

aneurysm, and the growth rate of an abdominal aortic aneurysm in these patients appears to be slower than in non-diabetic patients. [61] There is a strong genetic influence on the development of an abdominal aortic aneurysm in patients with Marfan syndrome and Ehlers-Danlos syndrome. [54] Furthermore, there is a strong correlation between hypertension, increasing aneurysm diameter and the risk of rupture. [58]

Physicians differentiate between pseudoaneurysms and true aneurysms. True aneurysms can be classified on the basis of morphological features into saccular aneurysms and fusiform aneurysms. These types of aneurysms can be seen in Figure 4. Arterial aneurysms are also classified according to their underlying aetiology: researchers have documented atherosclerotic aneurysms, syphilitic aneurysms, congenital aneurysms, mycotic aneurysms, traumatic aneurysms and vasculitic aneurysms. [51-53]

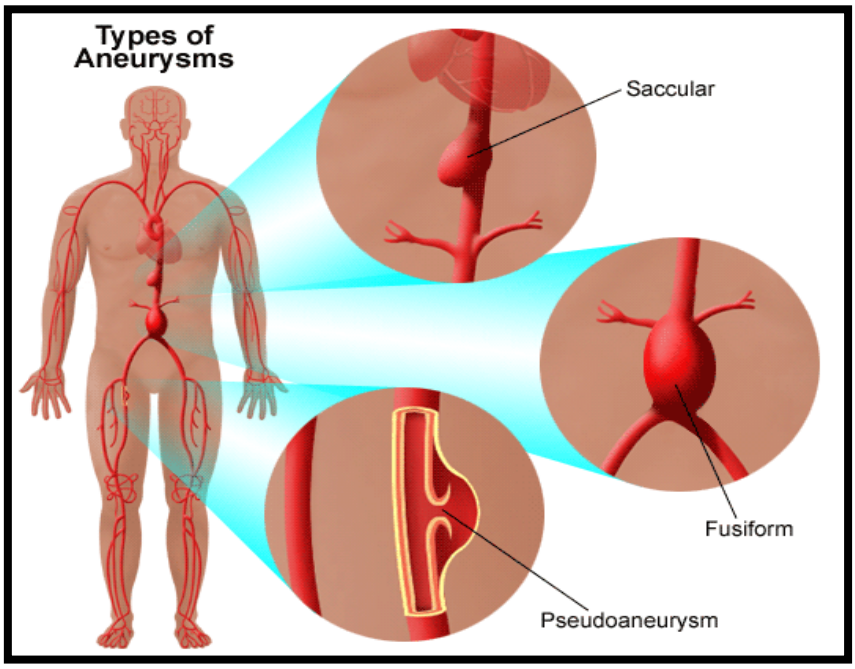

Figure 4: Types of aneurysms. [62]

A true aneurysm can be defined as a dilatation of all three layers of the artery, creating a large bulge of the arterial wall. In contrast, a pseudoaneurysm, or false aneurysm, is a contained rupture of the arterial wall that develops when blood leaks out of the arterial lumen through a hole in the tunica intima and tunica media and is contained by the tunica adventitia. Pseudoaneurysms form at sites of arterial injury

caused by infection or trauma, such as puncture of the artery during surgery or catheterisation. Pseudoaneurysms are extremely unstable and are prone to rupture. [51,53] They also differ from arterial dissection on the basis of causation. Pseudoaneurysms are mainly caused by accidental trauma or injury, whereas arterial dissections are caused by degeneration due to hypertension or disease. Pseudoaneurysms, as well as arterial dissections cause a separation of the layers of the arterial wall.

Aneurysms in the thoracic aorta are approximately five times less common than in the abdominal aorta. Aortic aneurysms may also spread to peripheral and cerebral arteries. [60,62]

Most aneurysms are asymptomatic, although some aortic aneurysm patients may be aware of the sensation of pulsation in the abdomen. Other patients present with symptoms associated with the compression of neighbouring structures by the expanding aneurysm; thoracic aortic aneurysms may compress the trachea or bronchi, resulting in cough, dyspnoea, or pneumonia. Compression of the oesophagus can result in dysphagia, and involvement of the recurrent laryngeal nerve may lead to a hoarse voice. Aneurysms of the ascending aorta may also dilate the aortic ring with consequential aortic regurgitation and symptoms of congestive heart failure. Abdominal aortic aneurysms may cause abdominal or back pain or nonspecific gastrointestinal symptoms. [51,53]

Age and sex feature distinctly among cardiovascular risk factors highlighting the importance of research on the influence these parameters have on arterial dimensions.

1.5 The role of genetics

The mechanical properties of arteries are independent factors for cardiovascular disease and mortality. [63,64] To understand the pathology of cardiovascular disease, the mechanical properties of the arterial wall, as well as the genetic influence on cardiovascular disease and mortality, should be kept in mind. [63,64]

Genetic factors may act either indirectly through age, hypertension, smoking, diabetes mellitus, and hyperlipidaemia, or directly affect the structure and function of the arteries. [63,64]

Although genetics play an important role and hereditary diseases such as Marfan syndrome and Ehlers-Danlos syndrome have been mentioned, the focus of this project was solely on the arterial variations based on clinical anatomy.

1.6 Variations in arterial dimensions in a South African cadaver population

During 2013, the variations in the arterial dimensions in a South African cadaver population were examined in a pilot study (97/2013). This study specifically evaluated the outer diameter, inner diameter and wall thickness, at 19 arterial sites (Table 1) in relation to age, weight, height, body mass index (BMI) and sex of a South African cadaver population.

Table 1: Arterial sites

#	Arterial site	Abbreviation
1	Ascending aorta superior to fibrous pericardium	AA
2	Abdominal aorta at level of celiac trunk	AC
3	Abdominal aorta before terminal bifurcation	AB
4	Left internal carotid artery distal to carotid body	LIC
5	Right internal carotid artery distal to carotid body	RIC
6	Left common carotid artery at origin	LCC
7	Right common carotid artery at origin	RCC
8	Left brachial artery before bifurcation	LBA
9	Right brachial artery before bifurcation	RBA
10	Left subclavian artery at origin	LSC
11	Right subclavian artery at origin	RSC
12	Left popliteal artery in popliteal fossa	LPA
13	Right popliteal artery in popliteal fossa	RPA
14	Left femoral artery at origin	LFA
15	Right femoral artery at origin	RFA
16	Left common iliac artery at origin	LCI
17	Right common iliac artery at origin	RCI
18	Left coronary artery at origin	LCA
19	Right coronary artery at origin	RCA

The 19 arterial sites measured were identified in order to represent all of the arteries of the human body. Elastic arteries close to the heart, defined as low-resistance pathways, as well as muscular arteries, more distally, active in vasoconstriction and less distensible, were included in the study. [25]

The relationships found between the independent variables and arterial dimensions are summarised in Table 2. The outer diameter (OD), inner diameter (ID) and wall thickness (WT) showed linear relationships with BMI at 94.7% of the measured sites. Of these linear relationships, the only inverse relationship was between the wall thickness of the ascending aorta and BMI. All other measurements showed positive relationships with BMI. Statistical significant differences were found between females and males, as well as between the left and right arteries, specifically the arteries of the heart and those of the upper and lower extremities.

Table 2: Relationship between arterial sites measured and demographic data

Arteries	BMI	Sex	Left and Right
Aorta			
Ascending	OD: +; WT: -; ID: +	OD: M>F*	
At celiac level	OD: +; WT: +; ID: +		
Before bifurcation	OD: +; WT: +; ID: +	ID: M>F*	
Common carotid	OD: +; WT: +; ID: +	No statistical significant difference	No statistical significant difference
Internal carotid	No linear relationship	No statistical significant difference	No statistical significant difference
Coronary	OD: +; WT: +; ID: +	No statistical significant difference	ID: L>R* OD: L>R*
Subclavian	OD: +; WT: +; ID: +	No statistical significant difference	ID: R>L*
Brachial	OD: +; WT: +; ID: +	No statistical significant difference	ID: R>L* OD: R>L*
Common iliac	OD: +; WT: +; ID: +	ID: M>F*	OD:R>L**
Femoral	OD: +; WT: +; ID: +	ID:M>F**	No statistical significant difference
Popliteal	OD: +; WT: +; ID: +	No statistical significant difference	ID: R>L* OD: R>L*

Includes negative (-) or positive (+) linear relationships with BMI and differences between male (M) and female (F), and left (L) and right (R) measurements. A statistical significant difference is indicated by *, and a marginal statistical significant difference is indicated by **.

The anatomical-morphological link between clinical problems related to cardiovascular diseases and arterial anatomy dimensions were demonstrated in the

pilot study. The decrease in the wall thickness of the ascending aorta associated with an increase in BMI is clinically important, as a thin aortic wall in association with an increased BMI may relate to clinical problems such as arterial aneurysm and arterial dissection. The enlarged outer diameter and inner diameter associated with an increase in BMI confirm that an increase in weight is an important factor in vascular ageing.

The larger arteries found in the upper and lower right extremities, as compared to the upper and lower left extremities, could possibly be related to limb dominance. Although this would be impossible to test in a cadaveric study, it would be a reasonable assumption, since these arteries mainly supply musculoskeletal elements. When muscles are regularly used, as would be the case in limb dominance, blood flow increases in direct proportion to the greater metabolic activity in the muscles, a phenomenon called active hyperaemia. [25]

This pilot study indicated that further research could establish the contribution of the various parameters to the outer diameter, inner diameter and wall thickness. This may help to indicate whether or not BMI contributes more to changes in the arterial dimensions than sex or age.

2 Aim and objectives

2.1 Aim

The purpose of this study was to evaluate the influence of specific parameters (age, weight, height, BMI and sex) on the variations in arterial anatomy in a South African population. A primary reference data set was compiled regarding these variations for a cadaver population. This primary reference data set will serve as the first step to a greater database of arterial measurements that could be sorted according to the above-mentioned parameters. In order to determine whether these results were an accurate reflection, a secondary data set was compiled for a living population and compared with the results from the cadaver population, specifically for the parameters of age and sex.

2.2 Objectives

The research objectives for this project were:

1. To determine the mean arterial dimensions (outer diameter, inner diameter and wall thickness) of the aorta and several other peripheral arteries in a South African cadaver population.
2. To correlate the mean arterial dimensions with changes in the relevant demographic factors (age, weight, height, BMI and sex) of a South African cadaver population.
3. To determine the mean arterial dimensions (outer diameter) of the aorta and several other peripheral arteries from a CT scan population, representative of a living South African population.
4. To determine whether the results for the outer diameter of the arteries at the 19 arterial sites from the two populations (paired according to age and sex) are comparable.
5. To compile a reference database regarding the range of the mean arterial dimensions for a South African population.

3. Materials and methods

3.1 Ethical clearance

Ethical clearance for this project (83/2014) was obtained from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria. Approval was also given by the Department of Anatomy, as well as the appropriate Postgraduate Committee of the Faculty of Health Sciences. The use of cadavers for the study falls within the auspices of the National Health Act 61 of 2003.

3.2 Study development and design

For the purpose of this study, a quantitative analytical study design was used. The cadaveric part of the study took place in the dissection halls in the Anatomy Department of the University of Pretoria, and the imaging part of the study took place in the Department of Radiology, Steve Biko Academic Hospital.

3.3 Procedures and criteria for selection

3.3.1 Cadaver study

A total of 104 embalmed cadavers were randomly selected from the Anatomy Department of the University of Pretoria, 54 cadavers in 2014 and 50 cadavers in 2015. The 50 cadavers measured at the University of Pretoria and the 36 cadavers measured at the Medunsa campus of the University of Limpopo during the 2013 pilot study (97/2013) were also included in the database. The demographic information related to each cadaver in the Department of Anatomy was obtained from the hospital records. BMI was calculated by weight in kilograms divided by height in meters squared. The weight and height were measured post-mortem, pre-embalmment and should therefore be an accurate reflection of the weight and height of the individual. The 190 cadavers were divided into two subgroups, 125 males and 65 females. Cadavers were not excluded due to height, weight or age. The age of the cadavers ranged from 20 to 99 years. Cadavers with known or visible arterial aneurysms, arterial dissections or those who have undergone previous vascular

surgery or suffered from any known vascular pathology were excluded from the study.

The arteries (Table 1) were exposed during the dissection sessions of medical, dentistry and medical sciences students within the Department of Anatomy. In cases where the arteries were not exposed, a basic dissection was done in order to find the relevant artery. Once the artery was identified, careful measurements were taken of the outer diameter using a standard stainless steel mechanical dial sliding calliper (accuracy 0.01 mm). This measurement was taken without compressing the artery and thereby confounding the results. Once the outer diameter (OD) was measured, the artery was sectioned and the wall thickness (WT) was measured at the same location. A simple mathematical formula (OD – 2WT) gave an indication of the inner diameter. A sample of the measurements was re-taken by the primary investigator in order to minimise intra-observer error. A sample of measurements was also re-taken by a separate individual, independent of the primary investigator, in order to minimise inter-observer error. As example, Figure 5 shows how the outer diameter of the ascending outer was measured, and Figure 6 shows how the inner diameter and wall thickness were measured.

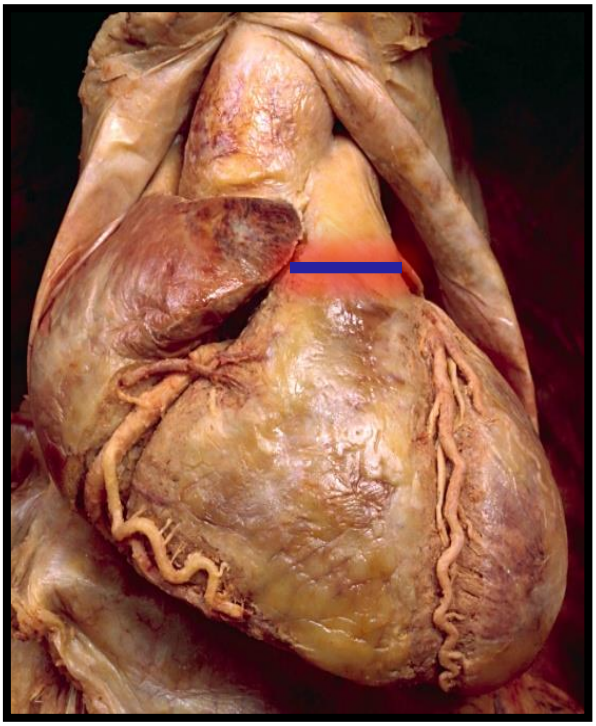

Figure 5: Example of an outer diameter measurement.

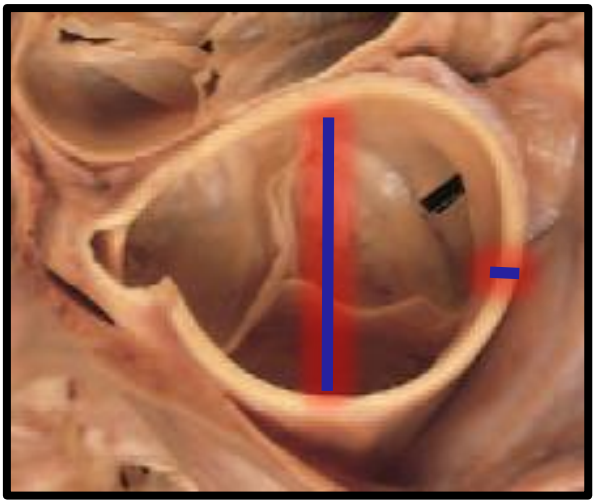

Figure 6: Example of inner diameter and wall thickness measurements.

3.3.2 Imaging study

Approximately 30 CT scans for each of the 19 arterial sites were retrospectively selected from the database of radiographic images at the Department of Radiology, Steve Biko Academic Hospital. Full-body CT scans are scarce and therefore the 30 CT scans for each of the 19 arterial sites were collected from 65 patients. The demographic information, related to each patient, was obtained from this database and included age and sex. In order to allow for comparisons to be made, CT scans of patients between the ages of 15 and 65 years, of both sexes were included. The CT scans of patients with known or visible arterial aneurysms, arterial dissections or those who have undergone previous vascular surgery or suffered from any known vascular pathology were excluded from this study.

RadiAnt, a Digital Imaging and Communications in Medicine (DICOM) viewer was used to analyse the CT scans. Using the on-screen measuring function, calibrated for each image, the outer diameter of each artery at the 19 identified sites was recorded. Because of difficulties visualising the arterial wall on CT scans, only the outer diameter of the arteries at each of the 19 sites was measured.

3.4 Statistical analyses

3.4.1 Cadaver study

Statistical analyses were done in order to determine the relationships between the outer diameter, inner diameter and wall thickness at the 19 arterial sites and the

demographic parameters (age, sex, weight, body length and BMI) of the cadaver sample. All statistical analyses were done with the assistance of a statistician.

Descriptive statistics was used to describe the data obtained from the sample, this includes the mean, median, standard deviation, minimum and maximum of all the measurements.

Comparisons between groups/measurements (i.e. left *vs.* right, male *vs.* female) were made using a paired *t*-test, while the strength of correlation between the collected measurements and the demographic details (age, weight, height and BMI) were tested using a correlation test (determined the correlation coefficient or R). Pearson Correlation tests were performed to determine the linear relationship between the continuous variables and arterial dimensions, and Spearman Correlation tests were performed to determine the linear relationship between the categorical variables and arterial dimensions.

In the cadaver study the dependent variables were the arterial measurements, while the independent variables were the age, sex, weight, body length and BMI of the sample.

3.4.2 Imaging study

Statistical analyses were done in order to determine the relationships between the outer diameter at the 19 arterial sites and the demographic parameters (age and sex) of the living sample. All statistical analyses were done with the assistance of a statistician.

Descriptive statistics was used to describe the data obtained from the sample, this includes the mean, median, standard deviation, minimum and maximum of all the measurements. Comparisons between groups/measurements (i.e. male *vs.* female) were made using a paired *t*-test, while the strength of correlation between the collected measurements (outer arterial diameter) and the demographic details (sex and age) were tested using a correlation test (determined the correlation coefficient or R). Pearson Correlation tests were performed to determine the linear relationship between the continuous variables and arterial dimensions, and Spearman

Correlation tests were performed to determine the linear relationship between the categorical variables and arterial dimensions.

In the imaging study the dependent variable was the outer arterial diameter, while the independent variables were the age and sex of the sample.

4. Results

4.1 Descriptive statistics

4.1.1 Cadaver study

Figure 7 represents the sex distribution of the cadaver sample. Measurements were taken on 190 cadavers; 125 males and 65 females.

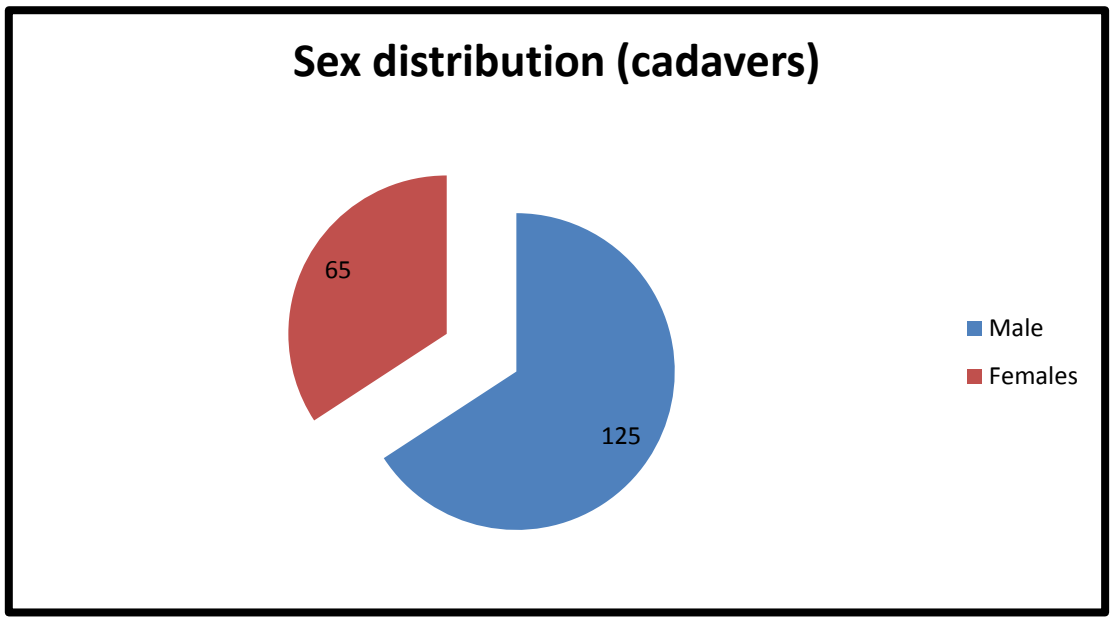

Figure 7: Sex distribution of cadaver sample.

Table 3 shows the descriptive statistics for the age, height, weight and BMI of the cadaver sample. Descriptive statistics includes the mean, median, standard deviation (SD), minimum and maximum values.

Table 3: Descriptive statistics for demographic parameters (cadavers)

Parameter	Mean	Median	SD	Minimum	Maximum
Age (years)	62.21	64.50	18.21	20.00	99.00
Height (m)	1.69	1.71	0.10	1.51	1.94
Weight (kg)	64.34	63.15	20.39	26.60	136.6
BMI (kg/m^2)	22.30	21.64	6.63	10.93	59.91

Figure 8 represents the age distribution of the 190 cadavers measured. As seen in Table 3, the minimum age was 20 years and the maximum age was 99 years. There were 12 cadavers for which the age was unknown.

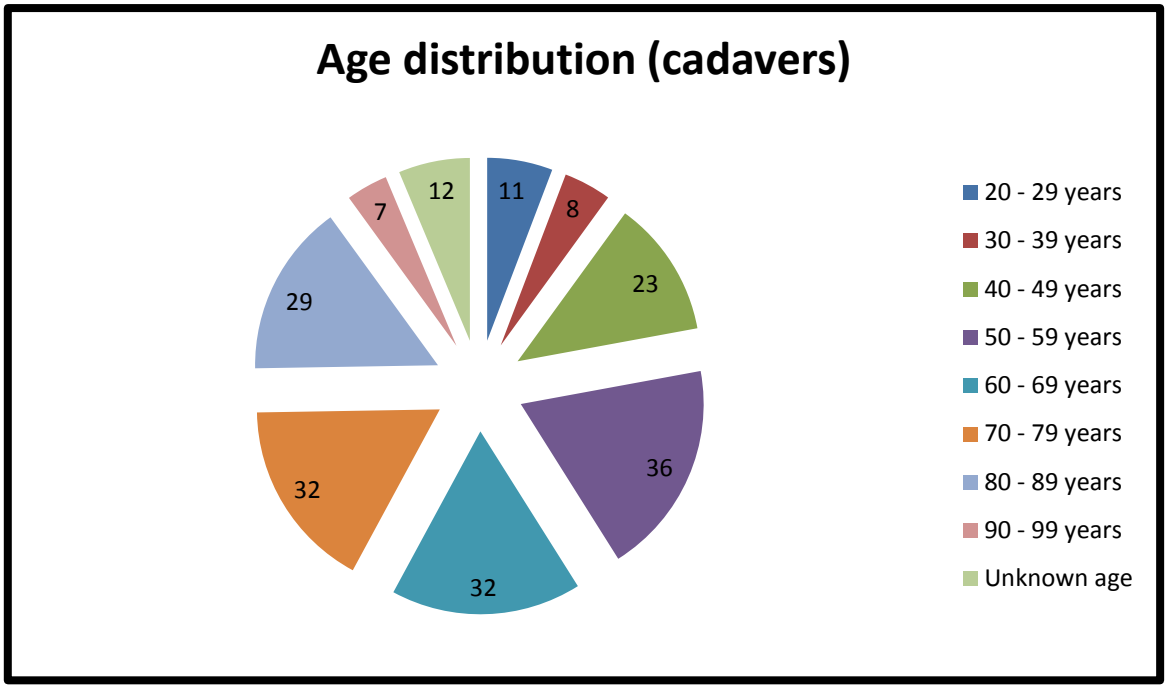

Figure 8: Age distribution of cadaver sample.

Figure 9 represents the height distribution of the cadaver sample. As seen in Table 3, the minimum height was 1.51 m and the maximum height was 1.94 m. There were 46 cadavers for which the height was unknown.

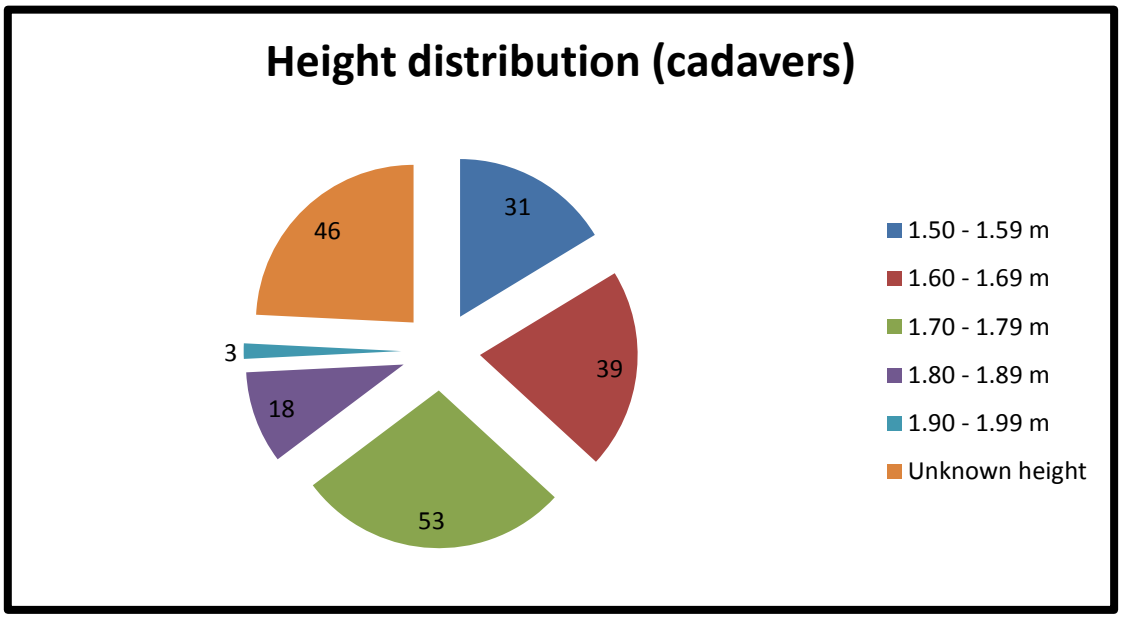

Figure 9: Height distribution of cadaver sample.

Figure 10 represents the weight distribution of the 190 cadavers measured. As seen in Table 3, the minimum weight was 26.6 kg and the maximum weight was 136.6 kg. There were 46 cadavers for which the weight was unknown.

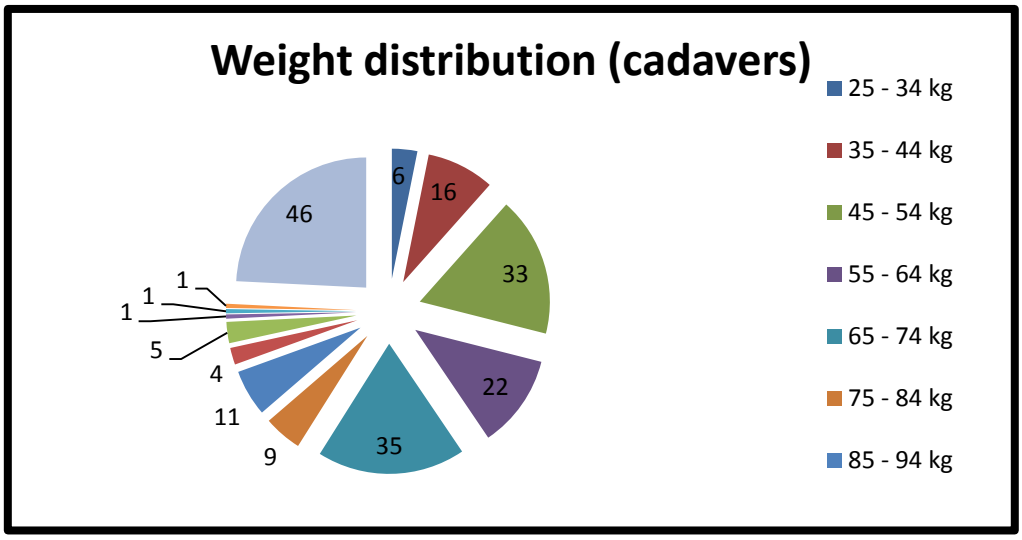

Figure 10: Weight distribution of cadaver sample.

Figure 11 represents the BMI distribution of the cadaver sample. As seen in Table 3, the minimum BMI was 10.93 kg/m^2 and the maximum BMI was 59.91 kg/m^2. A BMI lower than 18.5 kg/m^2 is considered underweight and a BMI between 18.5 kg/m^2 and 24.9 kg/m^2 is considered healthy. A BMI between 25 kg/m^2 and 29.9 kg/m^2 is considered overweight and a BMI above 30 kg/m^2 is considered obese. [65]

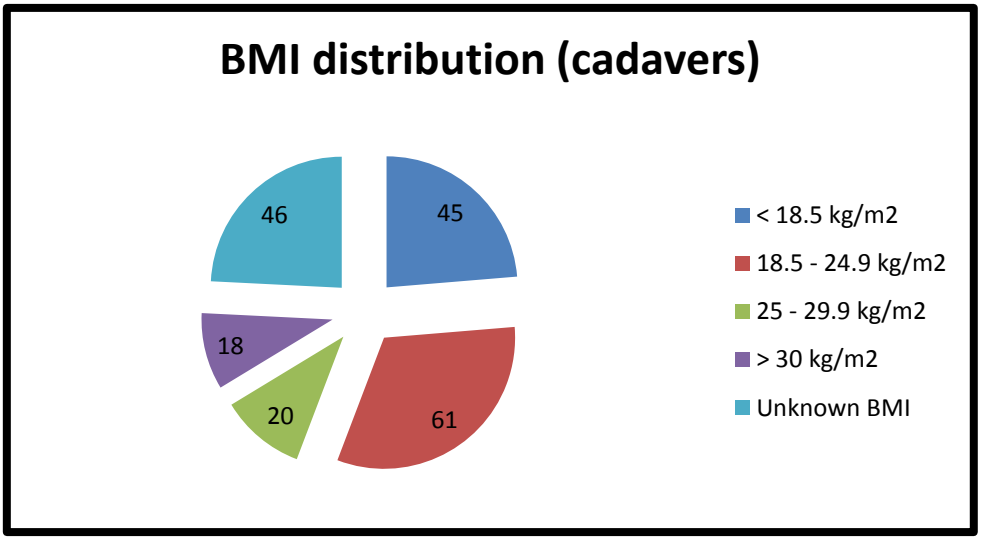

Figure 11: BMI distribution of cadaver sample.

Figure 12 represents the self-declared ethnicity, obtained from the hospital records, of the cadaver sample.

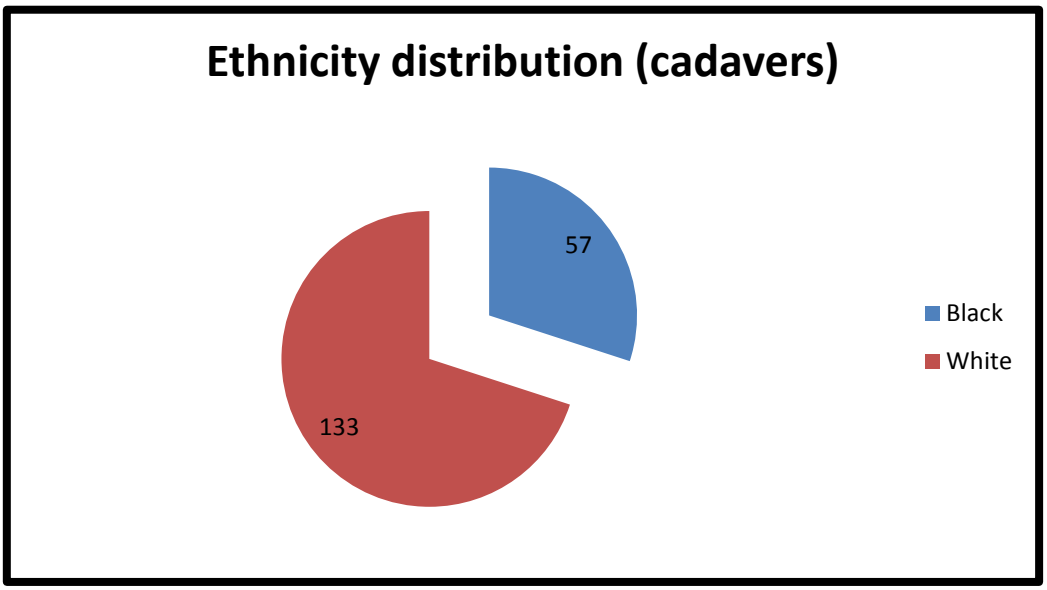

Figure 12: Ethnicity distribution of cadaver sample.

Table 4 shows the descriptive statistics for the outer diameter of the arteries measured in the upper - and lower extremities of the cadaver sample. Arteries measured in the upper extremities included the left brachial - (LBA) and right brachial arteries (RBA) and arteries measured in the lower extremities included the left popliteal - (LPA), right popliteal - (RPA), left femoral - (LFA) and right femoral arteries (RFA).

Table 4: Outer diameter of arteries of the extremities (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LBA	5.62	5.39	1.34	2.71	9.67
RBA	5.91	5.72	1.47	3.05	11.38
LPA	7.55	7.16	2.18	3.49	14.23
RPA	7.30	7.20	1.93	4.13	12.24
LFA	8.79	8.65	2.17	4.04	15.69
RFA	8.70	9.05	2.27	3.46	14.48

Table 5 shows the descriptive statistics for the outer diameter of the arteries measured in the neck of the cadaver sample. This included the left internal carotid - (LIC), right internal carotid - (RIC), left common carotid - (LCC), right common carotid - (RCC), left subclavian - (LSC) and right subclavian arteries (RSC).

Table 5: Outer diameter of arteries of the neck (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LIC	6.93	6.74	1.72	2.09	11.84
RIC	6.78	6.54	1.84	3.39	13.19
LCC	8.26	8.00	1.77	4.92	16.57
RCC	8.36	7.85	1.84	5.16	13.16
LSC	8.01	7.62	1.77	4.24	13.76
RSC	8.72	8.61	1.76	5.03	13.31

Table 6 shows the descriptive statistics for the outer diameter of the arteries measured in the thorax and abdomen. The ascending aorta (AA), left coronary - (LCA) and right coronary arteries (RCA) are arteries of the thoracic region and the aorta at the level of the celiac trunk (AC), the abdominal aorta just before terminal bifurcation (AB) and the left - (LCI) and right common iliac arteries (RCI), are arteries of the abdominal region.

Table 6: Outer diameter of arteries of the trunk (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
AA	30.70	30.20	6.60	16.48	49.52
AC	18.31	17.30	3.90	7.38	31.89
AB	18.65	18.63	3.38	8.55	31.48
LCI	11.56	11.32	1.86	7.76	16.52
RCI	11.88	11.61	2.16	6.70	17.82
LCA	5.41	5.28	1.87	2.09	21.04
RCA	4.37	4.16	1.19	2.09	8.49

Table 7 shows the descriptive statistics for the inner diameter of the arteries measured in the upper extremities of the cadaver sample.

Table 7: Inner diameter of arteries of the extremities (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LBA	4.87	4.76	1.35	2.07	8.65
RBA	5.19	5.03	1.42	2.51	10.08
LPA	6.44	6.07	2.10	1.85	12.26
RPA	6.18	6.15	1.87	1.87	10.88
LFA	7.56	7.54	2.18	3.55	14.38
RFA	7.32	7.24	2.11	2.48	13.10

Table 8 shows the descriptive statistics for the inner diameter of the arteries measured in the neck of the cadaver sample.

Table 8: Inner diameter of arteries of the neck (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LIC	5.94	5.92	1.69	1.31	10.94
RIC	5.75	5.45	1.74	2.35	11.87
LCC	6.93	6.74	1.65	3.86	11.91
RCC	7.02	6.70	1.76	3.47	11.62
LSC	6.87	6.67	1.54	3.58	12.54
RSC	7.51	7.50	1.64	3.89	11.73

Table 9 shows the descriptive statistics for the inner diameter of the arteries measured in the thorax and abdomen of the cadaver sample.

Table 9: Inner diameter of arteries of the trunk (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
AA	27.95	26.56	7.00	13.44	48.30
AC	16.32	16.18	3.63	5.34	26.65
AB	16.87	16.65	3.55	2.79	30.44
LCI	9.84	9.68	2.02	5.19	15.00
RCI	10.36	10.43	2.13	5.98	15.24
LCA	4.48	4.27	1.92	1.00	20.12
RCA	3.48	3.37	1.29	0.88	7.27

Table 10 shows the descriptive statistics for the wall thickness of the arteries measured in the upper - and lower extremities, of the cadaver sample.

Table 10: Wall thickness of arteries of the extremities (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LBA	0.37	0.34	0.17	0.05	0.92
RBA	0.36	0.34	0.16	0.04	0.84
LPA	0.55	0.51	0.33	0.05	1.79
RPA	0.56	0.48	0.36	0.01	2.72
LFA	0.62	0.59	0.29	0.13	1.95
RFA	0.70	0.62	0.40	0.10	2.68

Table 11 shows the descriptive statistics for the wall thickness of the arteries measured in the neck of the cadaver sample.

Table 11: Wall thickness of arteries of the neck (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LIC	0.50	0.44	0.24	0.07	1.79
RIC	0.51	0.47	0.26	0.12	1.62
LCC	0.66	0.58	0.31	0.10	2.33
RCC	0.67	0.61	0.31	0.10	1.97
LSC	0.57	0.47	0.34	0.13	1.98
RSC	0.61	0.56	0.30	0.17	2.30

Table 12 shows the descriptive statistics for the wall thickness of the arteries measured in the thorax and abdomen of the cadaver sample.

Table 12: Wall thickness of arteries of the trunk (cadavers)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
AA	1.37	1.23	0.72	0.06	4.89
AC	0.99	0.87	0.59	0.03	3.25
AB	0.89	0.74	0.54	0.19	2.88
LCI	0.86	0.71	0.49	0.16	2.60
RCI	0.76	0.70	0.37	0.08	1.82
LCA	0.47	0.41	0.29	0.09	1.74
RCA	0.45	0.40	0.27	0.05	1.51

4.1.2 Imaging study

Figure 13 represents the sex distribution of the CT scan sample. Measurements were taken on the CT scans of 65 patients; 45 males and 20 females.

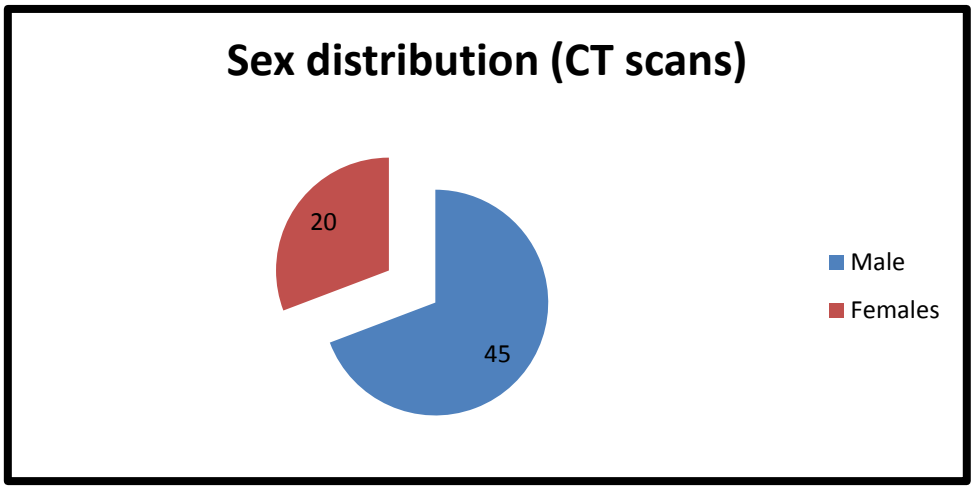

Figure 13: Sex distribution of CT scan population.

For the CT scan population, the mean age was 36.31 years and the median age was 35 years with a standard deviation of 11.99 years. The minimum and maximum age respectively was 15 and 65 years.

Figure 14 represents the age distribution of the 65 patients whose CT scans were measured. As seen in Table 13, the minimum age was 15 years and the maximum age was 65 years.

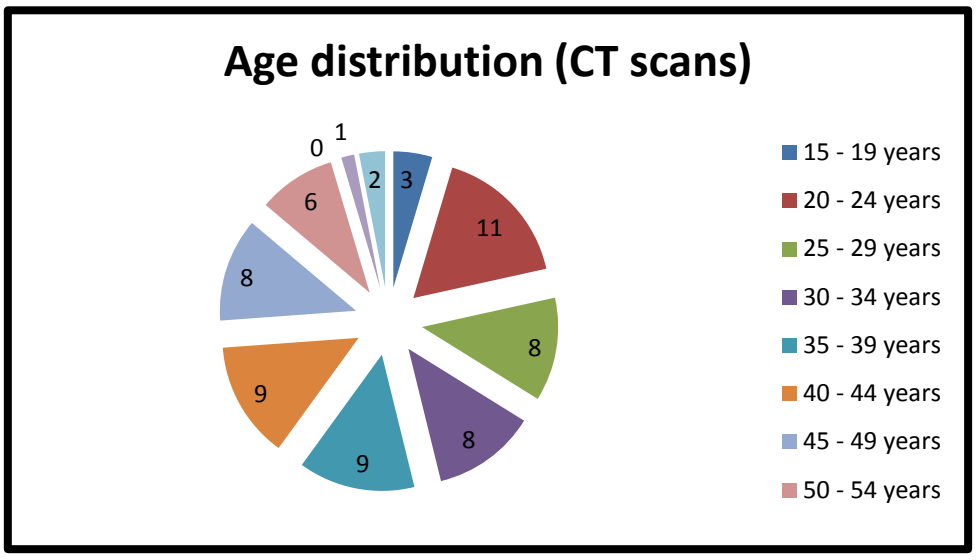

Figure 14: Age distribution of CT scan population.

Figure 15 represents the self-declared ethnicity, obtained from the CT scan, of the CT scan sample.

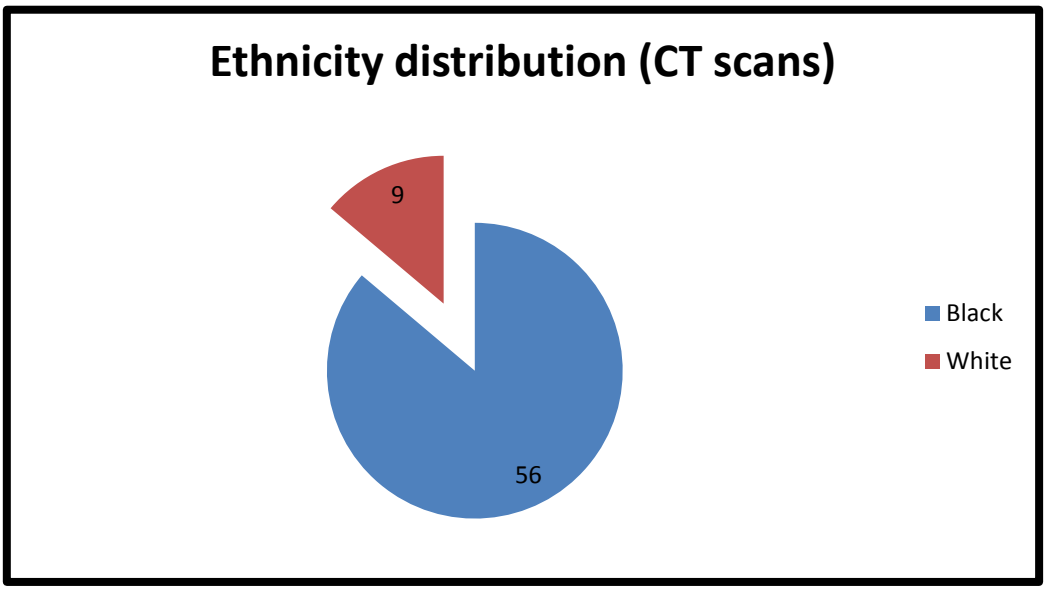

Figure 15: Ethnicity distribution of CT scan population.

Table 13 shows the descriptive statistics for the outer diameter of the arteries measured in the lower extremities of the CT scan sample. This included the left popliteal - (LPA), right popliteal - (RPA), left femoral - (LFA) and right femoral arteries (RFA).

Table 13: Outer diameter of arteries of the lower extremities (CT)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LPA	7.88	7.70	1.76	4.40	12.30
RPA	8.13	7.60	1.73	5.30	12.30
LFA	9.56	9.60	2.11	4.80	13.50
RFA	9.62	9.95	1.80	6.70	13.20

Table 14 shows the descriptive statistics for the outer diameter of the arteries measured in the neck of the CT scan sample. This included the left - (LIC) and right internal carotid arteries (RIC), the left - (LCC) and right common carotid arteries (RCC) and the left - (LSC) and right subclavian arteries (RSC).

Table 14: Outer diameter of arteries of the neck (CT)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
LIC	7.28	7.40	1.69	4.40	13.20
RIC	6.95	6.60	1.65	3.90	11.20
LCC	9.59	9.30	2.35	6.00	15.80
RCC	9.28	8.80	1.82	6.10	12.80
LSC	10.17	10.60	2.43	5.70	15.60
RSC	10.26	9.80	3.17	6.00	20.70

Table 15 shows the descriptive statistics for the outer diameter of the arteries measured in the thorax and abdomen of the CT scan sample. The ascending aorta (AA) and left coronary - (LCA) and right coronary arteries (RCA) are arteries of the thorax and the abdominal aorta just before terminal bifurcation (AB), the aorta at the level of the celiac trunk (AC) and the left - (LCI) and right common iliac arteries (RCI) are arteries of the abdomen.

Table 15: Outer diameter of arteries of the trunk (CT)

Parameter	Mean (mm)	Median (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
AA	23.59	23.80	3.88	13.80	32.10
AC	19.26	19.60	3.08	12.70	23.70
AB	17.81	17.60	2.34	13.50	22.60
LCI	10.60	10.80	2.25	5.80	16.30
RCI	11.09	11.00	1.73	7.30	14.70

4.2 Demographic parameters *vs.* arterial dimensions

Pearson Correlation tests were performed to determine the linear relationship between the continuous variables and arterial dimensions, and Spearman Correlation tests were performed to determine the linear relationship between the categorical variables and arterial dimensions. The cadavers for which height, weight or age were unknown, were not included in the Pearson Correlation tests, but were included in the Spearman Correlation tests if the sex was known.

Table 16 shows the contribution of the demographic data to the variation observed in the arterial dimensions of the upper - and lower extremities. Contributions more than 25% are shaded.

Table 16: Demographic contribution to variation in arteries of the extremities

	Contribution to variation (%)				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
LBA-OD	9.65	25.26	24.13	1.33	14.16
LBA-ID	7.26	17.58	16.33	5.17	12.71
LBA-WT	9.11	29.48	30.03	27.98	12.97
RBA-OD	13.47	26.91	24.77	19.09	22.92
RBA-ID	14.10	24.05	21.66	12.97	22.93
RBA-WT	0.00	17.45	18.13	30.14	5.01
LPA-OD	9.84	16.90	12.98	23.39	16.48
LPA-ID	12.16	18.59	13.82	14.90	19.59
LPA-WT	6.21	3.32	1.09	29.76	3.08
RPA-OD	14.44	14.08	9.49	15.21	14.56
RPA-ID	12.26	10.70	6.52	5.21	13.14
RPA-WT	6.75	9.79	8.38	26.65	2.15
LFA-OD	12.19	22.00	19.24	13.55	20.56
LFA-ID	15.38	23.97	20.01	5.52	19.90
LFA-WT	10.09	7.98	4.16	32.73	4.36
RFA-OD	22.94	17.20	7.41	10.76	32.48
RFA-ID	26.22	13.02	1.45	1.95	35.05
RFA-WT	0.50	16.67	17.88	26.06	0.37

Table 17 summarises the *P*-values of the contribution of the demographic data to the variation observed in the arterial dimensions of the upper - and lower extremities. A *P*-value smaller than 0.05 (shaded) indicated a statistically significant contribution.

Table 17: Significance of contribution to variation in arteries of the extremities

	***P*-value**				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
LBA-OD	0.2693	0.0034	0.0051	0.8649	0.0587
LBA-ID	0.4060	0.0430	0.0604	0.5066	0.0900
LBA-WT	0.2968	0.0006	0.0004	0.0003	0.0836
RBA-OD	0.1193	0.0016	0.0038	0.0132	0.0020
RBA-ID	0.1029	0.0050	0.0116	0.0939	0.0020
RBA-WT	0.9985	0.0429	0.0354	<0.0001	0.4981
LPA-OD	0.2832	0.0638	0.1558	0.0101	0.0709
LPA-ID	0.1838	0.0412	0.1306	0.1043	0.0313
LPA-WT	0.4989	0.7178	0.9058	0.0010	0.7371
RPA-OD	0.1141	0.1235	0.3007	0.0973	0.1111
RPA-ID	0.1803	0.2426	0.4776	0.5722	0.1508
RPA-WT	0.4618	0.2856	0.3611	0.0033	0.8147
LFA-OD	0.1639	0.0113	0.0271	0.1227	0.0180
LFA-ID	0.0784	0.0056	0.0214	0.5315	0.0222
LFA-WT	0.2496	0.3631	0.6357	0.0001	0.6195
RFA-OD	0.0079	0.0477	0.3965	0.3965	0.0001
RFA-ID	0.0023	0.1353	0.8682	0.8682	<0.0001
RFA-WT	0.9545	0.0551	0.0394	0.0394	0.9665

Table 18 shows the contribution of the demographic data to the variation observed in the arterial dimensions of the neck. Contributions more than 25% are shaded.

Table 18: Demographic contribution to variation in arteries of the neck

	Contribution to variation (%)				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
LIC-OD	10.33	15.91	12.5	24.63	28.23
LIC-ID	7.79	9.89	7.15	25.88	25.93
LIC-WT	9.43	22.28	19.77	3.12	20.02
RIC-OD	24.66	17.87	6.98	8.43	31.97
RIC-ID	23.36	14.92	42.05	2.60	28.91
RIC-WT	10.33	14.57	11.40	21.47	10.57
LCC-OD	5.43	35.26	36.20	12.64	8.69
LCC-ID	7.41	34.83	34.93	5.10	7.47
LCC-WT	3.77	8.07	10.29	21.63	3.46
RCC-OD	6.60	23.13	23.92	2.80	17.83
RCC-ID	9.53	19.21	18.59	2.68	18.87
RCC-WT	7.12	13.34	17.24	15.67	2.38
LSC-OD	3.57	4.20	3.45	29.34	21.63
LSC-ID	10.13	6.18	2.90	19.04	26.56
LSC-WT	11.62	2.44	2.26	32.78	3.47
RSC-OD	29.27	14.76	4.04	27.39	35.65
RSC-ID	27.66	9.62	0.37	22.56	35.16
RSC-WT	9.44	16.10	12.22	18.60	12.62

Table 19 summarises the *P*-values of the contribution of the demographic data to the variation observed in the arterial dimensions of the neck. A *P*-value smaller than 0.05 (shaded) indicated a statistically significant contribution.

Table 19: Significance of contribution to variation in arteries of the neck

	***P*-value**				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
LIC-OD	0.2461	0.0728	0.1598	0.0018	0.0002
LIC-ID	0.3819	0.2668	0.4226	0.0010	0.0008
LIC-WT	0.2900	0.0115	0.0253	0.6963	0.0099
RIC-OD	0.0052	0.0444	0.4358	0.4358	<0.0001
RIC-ID	0.0082	0.0941	0.6388	0.6388	0.0002
RIC-WT	0.2477	0.1022	0.2019	0.2019	0.1766
LCC-OD	0.5413	<0.0001	<0.0001	<0.0001	0.2555
LCC-ID	0.4043	<0.0001	<0.0001	<0.0001	0.3289
LCC-WT	0.6715	0.3632	0.2458	0.2458	0.6515
RCC-OD	0.4572	0.0084	0.0063	0.0063	0.0190
RCC-ID	0.2829	0.0292	0.0349	0.0349	0.0129
RCC-WT	0.4225	0.1319	0.0508	0.0508	0.7556
LSC-OD	0.6900	0.6396	0.7004	0.7004	0.0043
LSC-ID	0.2571	0.4903	0.7463	0.7463	0.0004
LSC-WT	0.1934	0.7856	0.8006	0.8006	0.6505
RSC-OD	0.0008	0.0963	0.6505	0.6505	<0.0001
RSC-ID	0.0016	0.2799	0.9673	0.9673	<0.0001
RSC-WT	0.2893	0.0702	0.1694	0.1694	0.0982

Table 20 shows the contribution of the demographic data to the variation observed in the arterial dimensions of the thorax and abdomen. Contributions more than 25% are shaded.

Table 20: Demographic contribution to variation in arteries of the trunk

	Contribution to variation (%)				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
AA-OD	1.82	20.64	19.68	47.70	0.63
AA-ID	1.03	17.63	17.75	41.74	0.15
AA-WT	11.87	5.90	1.53	15.69	10.03
AB-OD	35.59	23.36	8.17	11.59	41.29
AB-ID	39.05	23.20	7.00	4.58	43.06
AB-WT	17.28	3.38	2.45	21.08	3.46
AC-OD	2.72	28.99	31.47	42.78	5.13
AC-ID	2.61	33.35	36.24	42.08	2.55
AC-WT	0.98	5.97	6.59	12.49	1.95
LCA-OD	1.00	17.31	17.84	19.78	0.05
LCA-ID	2.88	13.50	12.09	13.87	1.57
LCA-WT	6.47	10.90	17.41	17.21	0.86
RCA-OD	17.42	18.29	11.31	8.93	15.66
RCA-ID	10.79	9.87	4.91	15.12	10.02
RCA-WT	12.33	16.44	12.98	17.08	8.60
LCI-OD	20.78	15.21	8.00	19.46	29.53
LCI-ID	21.07	10.78	3.27	1.76	27.54
LCI-WT	3.99	6.81	8.60	41.26	5.94
RCI-OD	31.19	26.49	14.03	13.80	37.40
RCI-ID	35.92	28.98	15.18	7.39	42.14
RCI-WT	12.83	6.5	2.90	19.24	11.27

Table 21 shows the *P*-values of the contribution of the demographic data to the variation observed in the arterial dimensions for the thorax and abdomen. A *P*-value smaller than 0.05 (shaded) indicated a statistically significant contribution.

Table 21: Significance of contribution to variation in arteries of the trunk

	***P*-value**				
Measurement	**Height**	**Weight**	**BMI**	**Age**	**Sex**
AA-OD	0.8394	0.0199	0.0266	<0.0001	0.9345
AA-ID	0.9088	0.0474	0.0459	<0.0001	0.9846
AA-WT	0.1839	0.5103	0.8647	0.0483	0.1918
AB-OD	<0.0001	0.0096	0.3712	0.2037	<0.0001
AB-ID	<0.0001	0.0101	0.4434	0.6166	<0.0001
AB-WT	0.0571	0.7118	0.7885	0.0198	0.6934
AC-OD	0.7616	0.0009	0.0003	<0.0001	0.5519
AC-ID	0.7707	0.0001	<0.0001	<0.0001	0.7671
AC-WT	0.9131	0.5053	0.4614	0.1617	0.8207
LCA-OD	0.9152	0.0643	0.0565	0.0183	0.9955
LCA-ID	0.7600	0.1502	0.1981	0.0998	0.8476
LCA-WT	0.4924	0.2462	0.0628	0.0406	0.9159
RCA-OD	0.0638	0.0514	0.2311	0.2956	0.0557
RCA-ID	0.2531	0.2963	0.6040	0.0766	0.2242
RCA-WT	0.1911	0.0805	0.1686	0.0444	0.2954
LCI-OD	0.0173	0.0828	0.3639	0.0265	0.0004
LCI-ID	0.0157	0.2202	0.7110	0.8427	0.0009
LCI-WT	0.6510	0.4397	0.3285	<0.0001	0.4841
RCI-OD	0.0002	0.0019	0.1045	0.1117	<0.0001
RCI-ID	<0.0001	0.0007	0.0789	0.3965	<0.0001
RCI-WT	0.1380	0.4566	0.7383	0.0259	0.1771

4.3 Left *vs.* right sided arteries

Table 22 summarises the *P*-values for the differences between the outer diameter of the arteries on the left and right side of the body.

Table 22: Outer diameter of left *vs.* right sided arteries

Arteries	*P*-value
Internal carotid	0.3763
Common carotid	0.5793
Brachial	0.2264
Subclavian	0.9694
Popliteal	0.1856
Femoral	0.5845
Common iliac	0.0798
Coronary	<0.0001

Table 23 summarises the *P*-values for the differences between the inner diameter of the arteries on the left and right side of the body.

Table 23: Inner diameter of left *vs.* right sided arteries

Arteries	*P*-value
Internal carotid	0.7143
Common carotid	0.3858
Brachial	0.4310
Subclavian	0.4141
Popliteal	0.2090
Femoral	0.7390
Common iliac	0.5299
Coronary	<0.0001

Table 24 summarises the *P*-values for the differences between the wall thickness of the arteries on the left and right side of the body.

Table 24: Wall thickness of left *vs.* right sided arteries

Arteries	*P*-value
Internal carotid	0.4978
Common carotid	0.7399
Brachial	0.6011
Subclavian	0.0915
Popliteal	0.2769
Femoral	0.0002
Common iliac	0.0011
Coronary	0.3063

4.4 Elastic arteries *vs.* muscular arteries

The average R-value of a selection of elastic arteries, were compared to the average R-value of a selection of muscular arteries. Table 25 shows the R-values for the elastic arteries. The correlation coefficient R, measures the strength and direction of a linear relationship between two variables - in this case; the correlation between the outer diameter of an artery and the age of the individual. The closer the R-value is to 1, the more closely the two variables are related.

Table 25: Elastic arteries

Arteries	R-value
AA	0.47695
AC	0.42781
AB	0.11588
LIC	0.24625
RIC	0.08430
LCC	0.12642
RCC	0.02800
LCI	0.19459
RCI	0.13803

Table 26 shows the R-values for the muscular arteries.

Table 26: Muscular arteries

Arteries	R-value
LFA	0.13554
RFA	0.10762
LPA	0.23389
RPA	0.15208
LBA	0.01327
RBA	0.19093
LCA	0.19783
RCA	0.08934

A positive R-value will always mean that the outer diameter will increase with increasing age. The higher the R-value the more oblique the gradient of the correlation will be when plotted using linear regression.

4.5 Cadaver measurements *vs.* CT scan measurements

To establish whether there is a statistical significant difference between the measurements of cadaver sample and the living sample, *t*-tests were performed. Cadavers and CT scan patients were matched for age and sex and 22 matching pairs were found. Cadavers were also matched to age alone and 29 matching pairs were found.

Table 27 shows the *P*-values found when comparing the cadaver measurements to the CT scan measurement for the specific age and sex matched pairs. A *P*-value smaller than 0.05 (shaded) indicated a statistically significant difference.

Table 27: Cadaver *vs.* CT scan measurements (age and sex)

Measurement	*P*-value
AA-OD	0.0665
AC-OD	0.6250
AB-OD	0.5000
LIC-OD	0.0547
RIC-OD	0.1914
LCC-OD	0.0156
RCC-OD	0.0742
LSC-OD	0.0273
RSC-OD	0.2188
LPA-OD	0.6250
RPA-OD	0.3500
LFA-OD	0.8125
LFA-OD	0.4375
LCI-OD	0.7500
RCI-OD	0.5000

Table 28 shows the *P*-values found when comparing the cadaver measurements to the CT scan measurement for the specific age matched pairs. A *P*-value smaller than 0.05 (shaded) indicated a statistically significant difference.

Table 28: Cadaver *vs.* CT scan measurements (age)

Measurement	*P*-value
AA-OD	0.0051
AC-OD	0.2500
AB-OD	0.4375
LIC-OD	0.1094
RIC-OD	0.2891
LCC-OD	0.0156
RCC-OD	0.0756
LSC-OD	0.0156
RSC-OD	0.2188
LPA-OD	1.0000
RPA-OD	0.1250
LFA-OD	0.8125
LFA-OD	0.4688
LCI-OD	0.8125
RCI-OD	0.8125

5. Discussion

5.1 Changes in arterial dimensions

Changes in arterial dimensions occur throughout life. Several researchers have found arterial size to be influenced by exercise, workload, body size, sex, nationality, ethnicity and age. [66-68] Arterial ageing is accompanied by a loss of compliance, and an increase in wall stiffness caused by structural changes such as the increase of collagen and cardiovascular complications. Hypertension, decreased wall thickness, and an increased inner diameter are some of the most important factors causing increased stress on the arterial wall that, in turn, could lead to undesirable clinical outcomes. [66-70]

The purpose of this study was to evaluate the influence of specific parameters (age, weight, height, BMI and sex) on the variations in arterial anatomy in a South African population. A data set was compiled regarding these variations in order to establish reference values for the normal arterial diameter for elastic, as well as muscular arteries specifically for a South African population. The thoracic – and abdominal aorta, common carotid -, internal carotid -, common iliac - and subclavian arteries are all considered elastic arteries. The brachial -, coronary -, femoral - and popliteal arteries are all muscular arteries.

5.2 Micro-anatomical structure of an artery

The collagen to elastin ratio varies extensively in the different parts of the human arterial system. Elastic fibres are the prevailing component in central arteries and collagen fibres are the prevailing component in peripheral arteries. The arterial system is divided in two major classes depending on the composition of the arterial wall: the elastic arteries and the muscular arteries. The central, elastic arteries have a large percentage of elastin components, larger diameter and are located closer to the heart, and the peripheral, muscular arteries contain a higher proportion of collagen and smooth muscle cells than elastic fibres and have medium-sized diameters. [71]

The arterial wall consists of three layers: tunica intima, tunica media and tunica adventitia. The tunica intima is the innermost layer and consists of a single layer of endothelial cells, and a sub-endothelial layer of elastin and collagen fibres that anchor the tunica intima to the internal elastic lamina. The internal elastic lamina consists of a fenestrated membrane of elastin that fuses the tunica intima and tunica media. The internal elastic lamina is more prominent in muscular arteries than in elastic arteries. [71]

The tunica media is the middle and the most important layer of the arterial wall. The mechanical properties of the wall are determined by the tunica media. In elastic arteries the tunica media consists primarily of elastic laminae interconnected with a network of elastic fibres. Between these laminae lie smooth muscle cells mostly parallel to the elastin, while some are oriented longitudinally. Collagen fibres bind the smooth muscle cells to the elastic laminae. In muscular arteries the tunica media consists primarily of smooth muscle cells. [71]

The outer layer, the tunica adventitia, is separated from the tunica media by the external elastic lamina. The tunica adventitia consists mostly of collagen, some elastin tissue that connects with surrounding connective tissue, small blood vessels (vasa vasorum), nerves and fibroblasts. [71]

The composition of the arterial wall influences the mechanical properties of arteries. The elastin to collagen ratio varies in the different areas of the arterial system and changes with increased age. Optimal proportions of elastin and collagen are present at a young age, but as age increases, collagen increases and elastin decreases, changing the movement of the arterial wall. The change results in increased arterial stiffness, decreased arterial distensibility and decreased arterial compliance. [70] According to researchers [59-64], these age-related changes are mainly seen in the central elastic arteries. Aortic stiffness is an independent predictor for cardiovascular mortality, stroke and coronary morbidity and mortality. [59-64, 71]

5.3 Variations in arterial dimensions in a South African population

5.3.1 Effects of ageing on arterial anatomy

Ageing leads to a number of changes in the arterial wall. Ageing of the arterial wall involves hyperplasia in the tunica intima and loss of the orderly arrangement of elastin fibres and laminae in the load-bearing tunica media. The thinning and degradation of elastin fibres are associated with an increase in collagen, and deposition of calcium is often seen. [54,55] Collagen is produced throughout life while elastin is not synthesised in older individuals, leading to increased arterial stiffness with age and a decreased arterial distensibility and arterial compliance. [61] Furthermore, the arterial diameter and wall thickness increase. [54] Arterial stiffness leads to an increased systolic blood pressure, which increases the workload of the left ventricle, as well as decreased diastolic blood pressure, which reduces coronary perfusion. [54,61]

For the South African population studied, it was found that age had a greater influence on the arterial wall thickness than the height, weight, BMI or sex. Table 16 shows that age contribute nearly 28% of the variation of the wall thickness of the left brachial artery, more than 30% of the right brachial artery, almost 30% of the left popliteal artery, about 27% of the right popliteal artery, almost 33% of the left femoral artery and 26% of the right femoral artery. Compared to height, weight, BMI and sex, age contributes the most to the differences seen in the wall thickness of the arteries in the neck and the trunk as seen in Table 18 and Table 20 respectively. As indicated by Tables 17, 19 and 21, the contribution of age is statistically significant.

Age showed a significant influence on 63% of the wall thickness measurements, on 47% of the outer diameter measurements and on 26% of the inner diameter measurements. Age also showed a positive linear relationship with outer diameter of these arteries.

5.3.2 Effects of sex on arterial anatomy

Researchers found a sex difference in arterial stiffness. Males are affected by a greater degree of arterial stiffness than females, and are more prone to a subsequent increase in cardiovascular morbidity and mortality earlier in life. [54]

Females appear to develop atherosclerotic plaque a decade later than males. At a similar age than their male counterparts, females show less atherosclerotic plaque. In successive age groups, the degree of inner diameter narrowing by atherosclerotic plaque was constantly and consistently lower in females than in male subjects. [72]

It is often stated that females have worse outcomes than men following a myocardial infarction and coronary revascularisation.[12] The reason for this is multifactorial, including the difference in the dimensions of the coronary artery; females have smaller arteries than males, as also seen in the current study. There is evidence linking smaller dimensions of the coronary artery to adverse cardiovascular events. In percutaneous revascularisation, coronary arterial diameter is a strong predictor of re-stenosis. Furthermore, in coronary artery bypass surgery, target vessel size correlates with long term graft patency. It is also known that in the event of atherosclerotic plaque rupture, a smaller inner diameter will increase the risk of total occlusion and myocardial infarction. [12]

Sex showed a significant influence on 63% of the inner diameter measurements, on 58% of the outer diameter measurements and only on 0.05% of wall thickness measurements in the current study.

Supporting the 2013 pilot study, the abdominal aorta before bifurcation, left and right internal carotid arteries, right common carotid artery, right brachial artery, left and right subclavian arteries, left and right femoral arteries and left and right common iliac arteries showed significant sexual dimorphism where arteries in females, were found to have smaller outer diameters. The outer diameters of the ascending aorta, aorta at the level of the celiac trunk, left common carotid artery, left brachial artery, left popliteal artery, right popliteal artery and left and right coronary arteries are also smaller in females although not statistical significantly.

The inner diameter of the abdominal aorta before bifurcation, left and right internal carotid arteries, right common carotid artery, right brachial artery, left and right subclavian artery, left popliteal artery, left and right femoral artery, and left and right common iliac arteries are significantly smaller in females. Although not significant, the inner diameters of the aorta at the level of the celiac trunk, left common carotid

artery, left brachial artery, right popliteal artery and right coronary artery are also smaller in females.

The wall thickness in females is significantly smaller in only the left internal carotid artery. The wall thickness is smaller, but not significantly, in the female ascending aorta, aorta at the level of the celiac trunk, abdominal aorta before bifurcation, right internal carotid artery, left and right common carotid artery, left brachial artery, right subclavian artery, right popliteal artery, left and right femoral artery, left common iliac artery and left and right coronary artery.

5.3.3 Effects of body size on arterial anatomy

Body size may confound the effect of sex on arterial dimensions because vascular surgeries may be more difficult in patients of smaller stature who may have proportionally smaller arteries. Smaller patients are likely to have shorter necks, which may limit surgical access to the common carotid - or internal carotid arteries. [73]

As parameters of body size, the effect of height, weight and BMI on arterial dimensions was studied.

5.3.3.1 Effects of height on arterial anatomy

Height showed a significant influence on 32% of the outer diameter measurements, on 32% of the inner diameter measurements and on none of the wall thickness measurements.

5.3.3.2 Effects of weight on arterial anatomy

Weight showed a significant influence on 58% of the outer diameter measurements, on 53% of the inner diameter measurements and on 16% of the wall thickness measurements.

5.3.3.3 Effects of BMI on arterial anatomy

As a function of both height and weight, BMI showed a significance influence on 37% of the outer diameter measurements, on 32% of the inner diameter measurements and on 21% of the wall thickness measurements.

5.3.4 Effects of ancestry on arterial anatomy

One would not be able to isolate the reason for any differences in ancestry, as the differences could possibly be accounted for by other socio-economic and socio-demographic factors – demographic features that were not available in the cadaver records and one that the researcher could not assume.

5.3.5 Left sided arteries *vs.* right sided arteries

For the outer diameter, the only arterial pair that showed a significant difference in size between the left and right side was the coronary arteries, with the left coronary artery being larger. This supports the finding of the 2013 pilot study. The inner diameter of the coronary arteries was also found to be significantly larger on the left. The thicker trunk and immediate bifurcation of the left coronary artery might explain this phenomenon.

The wall thickness of the femoral - and common iliac arteries shows a statistical significant difference between the left and right side of the body. The wall thickness of the right femoral artery and the wall thickness of the left common iliac artery are thicker.

The femoral – and common iliac arteries are prone to atherosclerosis, and this could possibly explain the thicker wall found here. [54] If not indicated in the records, it is impossible to determine whether the cadavers or CT scan patients suffered from atherosclerosis that could have accelerated age-related changes in the structure and function of arterial anatomy.

5.3.6 Elastic arteries *vs.* muscular arteries

The knowledge that the central, elastic arteries have a large percentage of elastin components, larger diameter and are located closer to the heart, and the peripheral, muscular arteries contain a higher proportion of collagen and smooth muscle cells than elastic fibres and have medium-sized diameters, fuelled interest in other possible differences between the two groups of arteries. [71]

Research has indicated that an abdominal aortic aneurysm is associated with abnormalities in the central, elastic arteries. [60] A difference in the rate of dilatation over time was considered as a possible explanation.

A two-sided *t*-test revealed no significant difference in the increase in the arterial diameter of the two groups of arteries with increase in age, and the null hypothesis of no significant difference was accepted. There is thus no significant difference in the rate of dilatation with age between the elastic and muscular arteries in a South African population that could help explain the prevalence of undesirable clinical outcomes in certain arteries.

5.3.7 Cadaver *vs.* CT scan measurement

The null hypothesis of no significant difference between the cadaver and CT scan measurements was accepted since the *P*-value indicated no significant difference for 87% of the measurements. The exceptions being the left common carotid - and the left subclavian arteries. These arteries are found on the left side of the neck, branches of the brachiocephalic trunk from the arch of the aorta. Since the origin of these two arteries differ from the origin of the same arteries on the right side of the neck, and it is the only two arteries showing a significant difference between cadaver and CT scan measurements (taken at origin), the notion that the embalming process might have affected the structure of the brachiocephalic trunk (and its branches) as the first branch of the arch of the aorta was considered. This is probably unlikely as the pressure or speed of the embalming process would've resulted in more differences between the two samples. It is possible that when comparing the cadaver measurements with a larger CT scan sample, the differences might not be significant. This theory will be tested in future studies.

5.4 Variations in arterial dimensions in non-South African populations

Da Silva *et al*. found the diameter of the distal abdominal aorta to vary according to age, sex, height, and degree of atherosclerosis on the aortic wall in a Brazilian population. [18] In a South African population, height contributed 36% to distal aortic variation, weight contributed 23%, BMI contributed 8%, age contributed 12% and sex

contributed 41%. The infrarenal aortic diameter was found to be greater in male cadavers than in female cadavers in the Brazilian population and in both sexes the infrarenal aortic diameter increased with age. Also, taller cadavers had larger aortic diameters. This was also found to be true for a South African population.

Patel *et al*. suggested that weight is an important risk factor in the process of vascular ageing, as shown by enlarged abdominal aortic and common iliac artery diameters. [19] As for a South African population, Patel *et al*. found the common iliac arteries and abdominal aorta before bifurcation to be larger in males, specifically when analysing the inner diameter of each artery.

Ilayperuma *et al*. highlighted sexual dimorphism in coronary arteries diameters in a group of adult Sri Lankans. [12] The diameters were smaller in females in comparison with males. This was also found to be true for a South African population.

In an East Indian population studied by Roy *et al.,* the left coronary artery shows a wide range of morphological variations, which is of great clinical importance. [74] Difficulties may occur during performance of diagnostic procedures, specifically during coronary artery surgeries or prosthetic valve replacements. [74] In the current South African population, the left coronary artery is significantly larger than the right coronary artery. For a South African population, weight contributed 17%, BMI contributed 18% and age contributed 20% to the arterial variation observed in the coronary arteries.

Dodge *et al.* studied a Seattle, USA, population and defined the normal inner diameter of the left coronary artery as 4.5 ± 0.5 mm for males and 3.9 ± 0.4 mm for females. The normal inner diameter for the right coronary artery was defined as 3.9 ± 0.6 mm for males and 3.3 ± 0.6 mm for females. [30]

Sass *et al*. found the strong correlations between age, morphologic parameters and arterial dimension to be dependent on sex and arterial site in a French population. [27]

In a Swedish population studied by Sandgren *et al.,* the inner diameter of the popliteal artery increases with age, initially during childhood growth, but also in

adults. This was found to be related to age and sex, with males having larger arteries than females. [75]

The mean femoral artery diameter of the same Swedish population was 9.8 mm in male subjects and 8.2 mm in female subjects. Contrary to the South African population, Sandgren *et al*. found no indication of sexual dimorphism for the femoral artery. Sandgren *et al.* found an increasing diameter of the femoral artery during growth, parallel to the increase in body size. At termination of childhood growth, male subjects have larger diameters than female subjects. [76]

Considering exercise, workload, body size, sex, ethnicity and age, Erbel *et al.* found the outer diameter of the elastic ascending aorta to expand by 1.3 ± 1.2 mm/year and the outer diameter of the descending aorta by 3.1 ± 3.2 mm/year in a German population. [67,69] The expansion results in an increased inner diameter along the entire length of the aorta. [69] The normal size of the aorta decreases with distance from the aortic valve in a tapering fashion. For this German population, the normal diameter of the ascending aorta has been defined as 37.1 ± 4 mm for males and 34.5 ± 4 mm for females. The normal diameter of the descending aorta has been defined as 28.2 ± 3 mm for males and 25.4 ± 3 mm for females. [70] An ascending aorta wall thickness of < 4 mm is regarded as normal. [70]

The current study found that in a South African population, the diameter of the ascending aorta tends to increase with age and an increase in BMI. However, body length and sex did not appear to have such a major effect on the ascending aortic diameter.

The phenomenon of an enlarged aorta with the advancement of age and a general increase in the size of peripheral arteries with an increase in BMI, occurs in all populations studied.

5.5 Assessing arterial dimensions in a clinical setting

When questioning the normal dimensions of an artery, textbooks and literature mostly provide different average values or ranges. Several factors such as age,

ethnicity, nationality and sex, viability of the subject (cadaver or living person), and measurement methods, which could be invasive or non-invasive, may explain this inconsistency.[77-81]

Quantifying arterial dimensions is of great significance in both research and in a clinical setting. Research commonly focuses on quantifying dimensional changes and measuring the percentage of stenosis in patients before and after intervention in order to define success and re-stenosis. In clinical practice, quantification of stenosis is used in the routine analysis of angiograms, and the results may influence diagnosis, restorative decisions and prognosis.[77-81]

There are numerous techniques to measure the arterial diameter. Measurements may be non-invasive radiological methods such as MRI, CT or ultrasound, or invasive methods using electronic or sliding callipers during operation, autopsy or in a cadaver. [78] In a cadaver, the arterial diameter can either be measured directly or after filling the arterial system with silicone, latex or oxide-gelatin. [78]

The most common methods for measuring the percentage of stenosis include visual inspection, sliding callipers, electronic callipers, quantitative angiography, and ultrasound. Visual inspection of diameters is of limited efficacy as changes in arterial diameter exceeding 30% are required for reliable detection. [77-81]

Visual grading of percentage of stenosis before and after intervention, results in a significant degree of inter- and intra-observer variability, and these inaccuracies can only be reduced by using a panel of observers. Quantitative angiographic analysis systems require offline digitisation, a process that can be costly and time consuming. Therefore, semi-quantitative methods like sliding callipers have been successfully used to quantify the severity of stenosis, and studies have shown good correlation between the use of callipers and quantitative angiography in measuring the percentage of stenosis. [77-81] In a living patient, high resolution ultrasound is probably the most practical and cost efficient way of measuring arterial diameter. This can be tested in future research endeavours.

5.6 Limitations

Limitations of this study include the possibility that the use of cadaveric tissue to measure the arterial diameter could yield measurements that do not accurately reflect a living population. Shrinkage and tissue distortion have been shown to be minimal, making cadaveric research possible and valid. [82] The arteries contain a high percentage of elastic tissue and smooth muscle in the tunica media, therefore arteries are not prone to collapse and should accurately reflect their true diameter. [25] The non-collapsing of arteries was validated by the results of no statistical significant difference between the cadaver and CT scan measurements with the exception of the left subclavian- and common carotid arteries.

If not indicated in the records, it is impossible to determine whether the cadavers or CT scan patients suffered from conditions such as elevated blood pressure, atherosclerosis, diabetes mellitus or high cholesterol during life. It is also unclear whether they were smokers or suffered from other risk factors that could have accelerated age-related changes in the structure and function of arterial anatomy. The use of a large cadaver sample over the course of the postgraduate study should minimise the influence these factors could have on the study.

Full-body CT scans are scarce and therefore the 30 CT scans for 15 of the 19 arterial sites were collected from 65 patients. The left and right brachial arteries and the left and right coronary arteries were not measured on the CT scans because these areas are only visible on a CT scan when specifically scanned, searching for pathology – pathology that could possibly influence the dimensions of these arteries. For future studies, the CT scan population will be enlarged, eliminating possible discrepancies leading to the differences found between cadaver and CT scan measurements.

5.7 The knowledge of arterial dimensions in a clinical setting

Researchers have found a correlation between dilated peripheral arteries and aortic aneurysmal disease. The diameters of the femoral -, popliteal -, brachial -, common carotid - and internal carotid arteries were measured in patients with aortic

aneurysms and it was found that the mean peripheral artery diameter was significantly higher at all measurement sites.[83,84] These findings support the hypothesis that patients with aortic aneurysmal disease have a generalised arterial dilation that may be unrelated to factors such as atherosclerosis. [83,84] The importance of screening for aneurysmal disease is well established, as is the greater risk attached to males, especially those over the age of 65 years. The relationship between arteriomegaly and the formation of aneurysms is now widely accepted. [85] Knowledge of the normal arterial diameter as a specific arterial site will assist in effective screening and can contribute to early diagnosis of cardiovascular complications such as aneurysmal disease.

In aortic valve disease, the pathology leading to valve replacement can alter the annulus diameter, resulting in annular stenosis or dilatation. The aortic annulus is the diameter at the base of the aortic root. In these situations, an important surgical decision is whether to adjust the size of the annulus to allow implantation of a normal sized valve or to use a replacement valve matching the diseased size. If the annulus size requires surgical modification, enlargement or reduction, anatomical guidelines are needed for determining how the diseased annulus should be resized. [86] An arterial anatomy reference data set can be utilised in the assessment of arterial changes.

Trans-catheter heart valve (THV) replacement is an emerging technology used to treat high-risk patients presenting with aortic stenosis. It is conceptually different from surgical aortic valve replacement in that the native valve is not excised but instead serves as the anchor for the implanted devices. An exact method for determining correct THV size is challenging because of the clinician's inability to visualise the valve directly. Consequently, adverse events related to under-sizing or over-sizing have occurred such as para-valvular leak, valve embolisation, coronary obstruction and injury to the aorta. This data set may have implications for valve sizing before THV implantation. [87]

Several researchers have correlated arterial diameter with anatomic variables (height, weight, age, sex, and body size). Despite differences in population groups,

sample size, specimen preparation, sizing methods, and measurement techniques, all these studies have identified correlations between growth of the body (with age, increased weight and increased height) and size of the arteries.

5.8 Future research

This arterial anatomy reference data set will provide a quantitative estimate of the severity of cardiovascular diseases in a South African population. Such a reference data set will aid in the assessment of arterial changes with age, as well as arterial dimensions within groups with different body sizes.

This arterial reference data set can benefit from further research and can be extended to include MRI or ultrasound measurements. An extensive arterial dimension reference data set for a South African population will provide better insight into the normal and abnormal diameters of the different arteries affected by cardiovascular disease. This knowledge can contribute to early diagnosis of various cardiovascular diseases and arterial abnormalities, specifically if the contribution or influence of the patient's demographic parameters (age, weight, height, BMI and sex) can be established.

6. Conclusion

This study found sexual dimorphism for the outer diameter and inner diameter of the abdominal aorta before bifurcation, left and right internal carotid arteries, right common carotid artery, right brachial artery, left and right subclavian arteries, left and right femoral arteries and left and right common iliac arteries where females have smaller arteries. The wall thickness of the left internal carotid artery is the only wall thickness measurement statistically smaller in females.

Body size - weight, height and BMI – influences the arterial dimensions of all arteries studied. Body size especially showed a significant contribution to the dimensions of the aorta, common iliac arteries, subclavian arteries and brachial arteries.

A statistical significant increase in diameter was found with age, but no statistical significant difference was found in the increase in the arterial diameter of elastic – and muscular arteries with increased age.

As expected, the coronary arteries showed a statistical significant difference between left and right. The thicker trunk and immediate bifurcation of the left coronary artery possibly explain the larger diameter found. The absence of the statistical significant difference between the left and right brachial and left and right popliteal arteries as found in the 2013 pilot study, then attributed by limb dominance, can be explained by the substantially larger sample size.

No statistical significant difference was found between cadaver measurements and CT scan measurements with the exception of the left subclavian – and left common carotid arteries. These arteries, originating from the brachiocephalic trunk, the first branch of the arch of the aorta, could possibly be influenced by the speed or pressure of the embalming process, but this should be further investigated by comparing the cadaver measurements to a larger CT scan sample.

Therefore, with the exception of two measurements, measurements in cadavers and living people are interchangeable and concerns regarding the effect of distortion and shrinkage as quoted by advocates against cadaver studies are unfounded.

Arterial pathology is a major contributor to cardiovascular disease and mortality. Data on normal arterial dimensions for a South African population is scarce, but essential when evaluating whether a dilatation or stenosis are pathological. This study supports other research indicating an age-related increase in the dilatation of the arterial lumen. [13-17,19,21,22,26,27] The arterial diameter is therefore a useful indicator of the vascular ageing process. As also found in other populations studied, the principle dimensional changes that occur with vascular ageing in a South African population are arterial dilatation and increase in wall thickness. [26-28]

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