MORPHOLOGICAL AND HISTOLOGICAL ANALYSIS OF VASCULAR CONDUIT OPTIONS USED FOR CORONARY ARTERY BYPASS GRAFTING - A SOUTH AFRICAN PERSPECTIVE

BY

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Declaration

I, Sandile Ntando Ntuli, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. Any contributions to and quotations in the dissertation have been cited and referenced.

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ABBREVIATIONS

AICA	Anterior Interventricular Coronary Artery
AIDS	Acquired Immunodeficiency Syndrome
CABA	Clinical Anthropology and Biological Anthropology
CAGB	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CVD	Cardiovascular disease
CX	Circumflex Artery
EEL	External Elastic Lamina
GSH	Groote Schuur Hospital
HIV	Human immunodeficiency virus
IHC	Ischemic Heart Disease
IEL	Internal Elastic Lamina
IEA	Inferior Epigastric Artery
ILWH	Individuals living with HIV
LCA	Left Coronary Artery
LDL	Low density lipoprotein
LITA	Left internal thoracic artery
NCD	Non-communicable diseases
PI	Primary Investigator
PICA	Posterior Interventricular Coronary Artery
RA	Radial Artery
RCA	Right Coronary Artery
RGEA	Right Gastroepiploic Artery

RITA	Right internal thoracic artery
ROS	Robot Operating System
SSA	Sub-Saharan Africa
SV	Saphenous Vein
TA	Tunica Adventitia
TI	Tunica Intima
TM	Tunica Media

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ABSTRACT

Background: Cardiovascular disease is the leading cause of death worldwide and coronary artery disease (CAD), largely attributed to occluded coronary arteries, is the most common cardiovascular disease. Coronary artery bypass grafting (CABG) is considered the gold standard invasive intervention to treat CAD. This procedure involves grafting a blood vessel from elsewhere in the body to the affected coronary artery to bypass the site of occlusion. The vascular conduit may be obtained from various sites. CABG is one of the most effective and lasting therapies for CAD; however, an important decision for the surgeon to make is which vessel to use as a conduit. The aim of this study was to determine which conduit is the most morphometrically and histologically similar to coronary arteries.

Methodology: The objectives of this study were met through a cross-sectional study design. The first approach was conducted on vascular conduits from the Department of Human Biology's donor sample, at the University of Cape Town (UCT), and angiographic images from the Cardiac Clinic, at Groote Schuur Hospital (GSH). The typical parameters of coronary arteries were measured, including the arteries of individuals with CAD, with the latter cohort necessary for purposes of establishing a standard. The parameters which were measured were: length, luminal diameter, and wall thickness (i.e. width of histological layer). A similar approach was used for the measuring the following vascular conduits: saphenous vein (SV), right and left internal thoracic artery (RITA/LITA), inferior epigastric artery (IEA), right gastro-epiploic artery (RGEA), and the radial artery (RA). The second approach involved cardiothoracic surgeons were surveyed regarding their decision-making before performing CABG surgery. A quantitative survey was circulated amongst South African cardiovascular surgeons to establish objective factors that affect vascular conduit choice. The questionnaire was composed of multiple choice and Linkert scale type questions.

Results: The normal mean RCA length and diameter was 11.39±3.11 cm and 0.30±0.08 cm respectively, in males. For females the RCA length and diameter was 12.61±2.78 cm and 0.26±0.07 cm. The LCX had a mean length and diameter of 8.64±2.18 cm and 0.24±1.10 cm respectively for males. In females the mean length was 9.27±2.94 cm and the diameter was 0.21±0.07 cm. The AICA had a mean length and diameter of 12.06±4.22 cm and 0.25±0.08 cm respectively in males. In females the mean length and diameter was 12.84±3.34 cm and 0.20±0.07 cm, respectively. The LITA had a longer length, relative to the RITA when compared to 4 out of 5 coronary artery types, the only exception was the AICA. The mean wall thickness of the SV is 127.97±34.99 um. The mean diameter of the SV is closely related to the RCA, LCX, PICA and AICA. The respondents of the survey were from both private and public hospitals, with experience ranging from 5 to 20+ years. The SV was preferred mostly for emergencies due to easy access, while the LITA was most preferred when used individually.

Discussion: Length variance of coronary arteries is independent from sex and age, the only mean differences are found between populations. The diameter size is affected by sex, age and the presence of a pathology. This is attributed to human variation between the different sexes and the changes on the vascular system due to progressive age. Diameter and wall thickness are the prevalent factors that affect patency while length contributes to a conduits' suitability for handling during surgery.

Conclusion: The LITA, RA and SV are the three most suitable grafts although more work must be done to compare the patency of the RA compared to the LITA and RITA used in bilateral grafts. The RITA is similar to the RGEA but depending on the coronary artery that is occluded, one might be more suitable than the other. The IEA is the least most suitable graft.

Key words: coronary artery disease, CABG surgery, histological, inferior epigastric, internal thoracic artery, morphological, radial artery, right gastro-epiploic artery, saphenous vein

CHAPTER 1: INTRODUCTION

1.1 THE CARDIOVASCULAR SYSTEM

The cardiovascular system (CVS) plays an essential role in cellular metabolism mainly through the transportation of oxygen and nutrients, and the removal of metabolic waste from tissues. It also plays crucial roles in thermoregulation, immunology and biochemical mediations within the body (Hall and Hall, 2020). The heart is the pillar on which the cardiovascular system relies on for optimal function. It acts as a pump which mediates circulation in response to the body's needs. The heart, like many of the tissues in the body, is also heavily reliant on the vascular system for adequate supply of oxygen and nutrients to ensure the survival of its own myocardial tissue (Conti, 2013).

The right coronary artery (RCA) and the left coronary artery (LCA) are the two main arterial blood supply vessels of the heart. These vessels originate on the superolateral aspect of the proximal ascending aorta (Hansen, 2017). The RCA supplies both the right atrium and ventricle; including the sinoatrial and atrioventricular nodes which regulate heart rhythm (Chruścik et al., 2021) [Figure 1.1a].

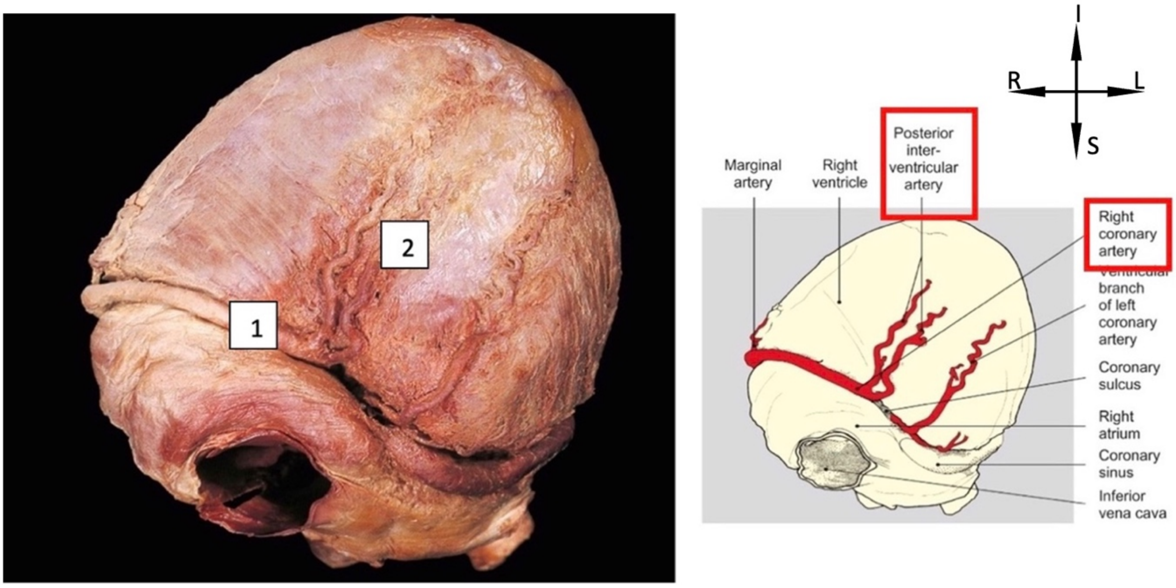


Figure 1.1a: Views of the posterior surface of the heart, with the apex situated superiorly. On the left, coronary arteries are labelled 1: right coronary artery and 2: posterior interventricular artery. On the right, the posterior interventricular artery and right coronary artery labelled in red blocks (Gosling et al., 2017).

(Key: L: left; R: right; I: inferior; S; superior)

The anterior interventricular coronary artery (AICA) is a branch of the LCA, and it supplements the RCA's blood supply to the anterior surface, specifically at the septal regions of the heart. The AICA also supplies the left atrium and ventricle (Berdajs and Turina, 2011). The circumflex artery is the second branch of the LCA, and it supplies the lateral and posterior surfaces of the myocardium [Figure 1.1b]. Smaller branches, like the diagonal and right marginal branches, assist with reaching other aspects of the heart which ensures adequate vascularization (Loukas et al., 2013).

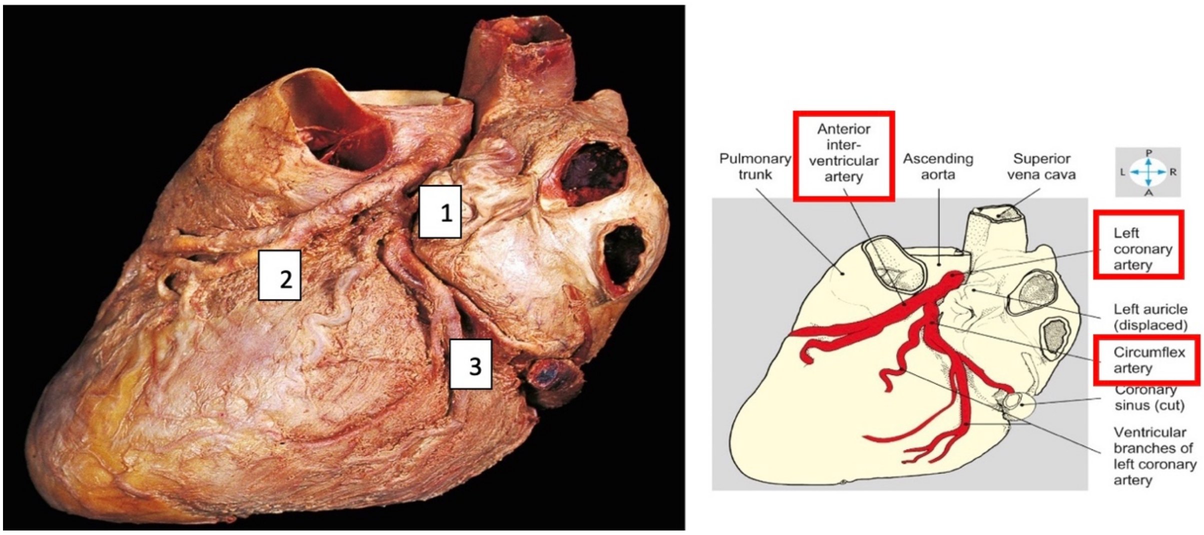


Figure 1.1b: The sternocostal surface of the heart. In the image on the left, the coronary arteries are labelled 1: left coronary artery; 2: anterior interventricular artery; and 3: circumflex artery. In the image on the right the left coronary artery, anterior interventricular artery and circumflex artery are labelled in red blocks (Gosling et al., 2017).

(Key: A: anterior; L: left; P: posterior; R: right)

The posterior interventricular coronary artery (PICA) is often described as originating from the RCA, however, in certain instances it may emerge from the circumflex artery (CX), a branch of the LCA (Moore et al., 2013). A variation in the origin of the PICA plays a determinative role on a phenomenon called circulatory dominance. There are three types of circulatory dominance: right, left and co-dominant circulation (Parikh et al., 2012). Right and left circulatory dominance is determined by the origin of PICA from the RCA or the CX, respectively. Co-dominant circulation occurs due to an equal supply of the posterior interventricular septum by both the RCA and circumflex artery (Shahoud et al., 2019). Right dominant circulation is more prevalent than left and co-dominant circulation, although all three variants are considered normal (Reddy and Lokanadham, 2013). Variations in the course and origin of coronary arteries are common and well described in literature (Loukas et al., 2013, Kosar et al., 2009). While the macroscopic anatomy is well known, little is known about the variations occurring at a histological level.

Arteries are composed of three histological layers: the tunica intima (TI), tunica media (TM), and tunica adventitia (TA). Furthermore, two elastic layers called the internal elastic lamina (IEL), and the external elastic lamina (EEL) are situated on the inner and outer surfaces of the TM, respectively (Bradbury, 2014) [Figure 1.2].

Each layer has distinctive cellular features that respond to the extrinsic and intrinsic environment. The TI lines the lumen of the artery and is composed of smooth endothelium that aids in endocrine function, usually through initiating and mediating biochemical responses that affect the blood and the TM (Yang et al., 2018). The TM is composed chiefly of smooth muscle cells whilst the TA contains loose connective tissue made from collagen fibres and fibroblasts (Burris and Shoukfeh, 2015). Arteries are either muscular or elastic depending on the dominance of smooth muscle cells (SMC) in the TM. Elastic arteries are generally larger, containing more elastic fibres than SMC in the TM, and they are situation closer to the heart. Coronary arteries are muscular arteries (Tucker et al., 2017). When pathologies or trauma occur in arteries, the net effect may alter the normal anatomy and physiology of the vessel at a microscopic and macroscopic level (van der Wal, 2007).

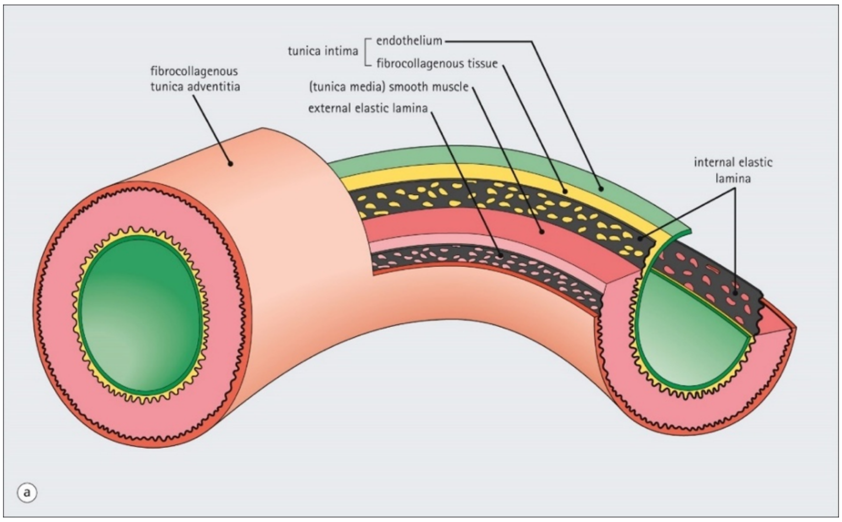


Figure 1.2: Typical artery depicting the tunica intima, tunica media, and the tunica adventitia and their associated cellular structures (Lowe et al., 2020).

Traditional investigations on the variations of the vasculature of the heart tend to focus on coronary artery lengths and luminal diameters, usually in relation to inter-population studies or sex-based differences. The least evaluated parameter in literature is variation in the thickness of the histological layers of arterial walls (Martínez-González et al., 2017). This has clinical implications since the histology, size, and function of an artery has a direct correlation to its susceptibility to remodelling or degeneration (Wang and Tian, Cameron et al., 2003, Jiang et al., 2017). An example of this principle can be demonstrated by the higher prevalence of aneurysms in the aorta compared to coronary arteries (Jiang et al., 2017). Conversely, coronary arteries are more susceptible to pathologies that lead to acute occlusion compared to large elastic arteries like the aorta (Crawford et al., 2014). Understanding the vascular anatomy of the heart is critical when clinicians consider appropriate remedies for patients with cardiovascular diseases (Berdajs and Turina, 2011).

1.2 CORONARY ARTERY DISEASE

Cardiovascular diseases (CVD) are a leading cause of mortality with a third of deaths worldwide being attributed to it (Bauersachs et al., 2019). This prevalence is mostly concentrated in first-world countries, with the most common manifestation of CVS disease being coronary artery disease (CAD); also known as coronary heart disease (Sanchis-Gomar *et al.*, 2016). CAD is mainly caused by atherosclerosis. Atherosclerosis is defined as pathophysiology characterized by plaque formation due to a progressive accumulation of fatty deposits in the luminal surface of the arterial wall (Gustafson, 2010). The severity of the plaque build-up can lead to the occlusion, narrowing, or hardening of the heart's vessels resulting in obstructed blood flow (Herrington et al., 2016, Martínez-González et al., 2017). A patient with CAD may experience no symptoms or, in mild-to-severe cases, angina and myocardial infarction. The extent and severity of an occlusion dictates the type of treatment needed. Treatments range from the use of pharmaceuticals, percutaneous coronary intervention (angioplasty with stent), or coronary artery bypass graft (CABG) surgery (King et al., 1994, Elisaf, 2001).

Clinical interventions for CAD primarily aim at alleviating symptoms and restoring vascular function to prevent myocardial ischemia and infarction (Kleisli et al., 2005). Subject to the extent of the occlusion, the use of angioplasty and CABG surgery are considered standard treatments worldwide (Michaels and Chatterjee, 2002). Techniques used in angioplasty vary; ranging from a balloon-tipped catheter that broadens the narrowed arterial wall, to devices that directly trim the plaque away. Thereafter, a stent (a wire-mesh tube) is used to reinforce the weakened area of the blood vessel. This intervention has been historically preferred by most clinicians and patients since it is non-surgical and low risk in terms of operative complications (Serruys et al., 2009). However, the risk of restenosis around the stent has become more apparent in cases where patients do not adhere to the prescribed lifestyle changes or pharmaceuticals (Michaels and Chatterjee, 2002). These considerations made CABG surgery the gold-standard for treating CAD in recent decades (Rocha, 2017).

CABG surgery involves the use of vascular conduits that bypass an occluded coronary artery distally with the intention to achieve revascularization of the myocardium (Bachar and Manna, 2018) [Figure 1.3]. The success of CABG, like many surgical operations, can be measured by a post-operative improvement in the quality of life and life-span (Stone et al., 2019). A major determining factor is the patency of the graft used. Vascular conduits that are commonly used in CABG are the left and right internal thoracic artery (ITA), radial artery (RA), ulnar artery (UA), right gastroepiploic artery (RGEA), inferior epigastric artery (IEA), and the saphenous vein (SV) (Gharibeh et al., 2021). Since the inception of the of CABG surgery the appropriateness of a specific vascular conduit over others has been debated (Martínez-González et al., 2017).

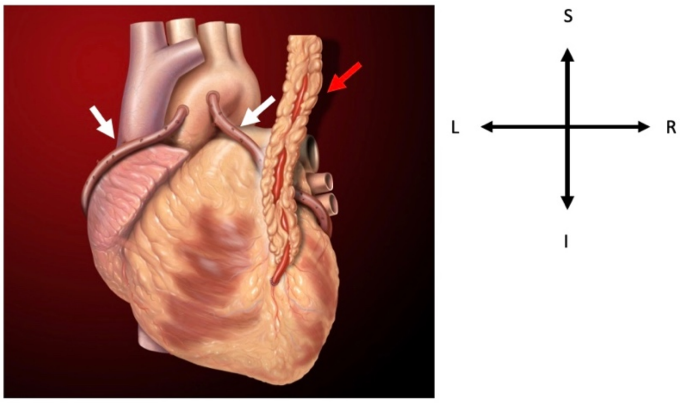


Figure 1.3: The left internal thoracic artery (red arrow) grafted on the LCA; as well as two saphenous vein grafts (white arrows) after CABG (Bachar and Manna, 2018).

(Key: I: inferior; L: left; R: right, S; superior)

In developed countries CABG surgery has contributed to a significant decrease in CAD related mortality (Frohlich and Al-Sarraf, 2013). This trend is not evident for developing countries, which have shown a rising incidence of CABG-related deaths (Okrainec et al., 2004).

1.3 THE INCREASING PREVALENCE OF CAD IN SOUTH AFRICA

The prevalence of CVD in Sub-Saharan Africa has increased due to changes in lifestyle behaviours (Mensah et al., 2015, Hamid et al., 2019). CAD is amongst the most prevalent CVD and a common cause of mortality in South Africa alongside dominant communicable diseases like HIV/AIDS and Tuberculosis (Abdelatif et al., 2021). This indicates that South Africa's healthcare burden has shifted from being traditionally confined to communicable diseases, to non-communicable diseases (NCD) like CVD (Hamid et al., 2019).

Studies in South Africa have predominantly focused on the ethnic-related prevalence of CAD (Swart et al., 2005). Consequently, there is limited epidemiological evidence on its prevalence in urban versus rural areas. This is crucial since socioeconomic statuses can impact access to CABG surgery, medical advice on risk management, and nutrition necessary for a diet that could promote cardiovascular health (Abdelatif et al., 2021).

1.4 POSTOPERATIVE OUTCOMES IN SOUTH AFRICANS WHO HAVE UNDERGONE CABG SURGERY

Negative postoperative outcomes following CABG surgery are generally low, with the USA and most European countries reporting rates of 1-4%, which is similar to the private healthcare sector in South Africa (Swart et al., 2005). In some South African public hospitals this figure is over 10% although it remains unclear why this discrepancy exists. Negative outcomes are attributed to factors such as population-age, comorbidities, and other perioperative complications (Reiche et al., 2021). Amongst the many areas of interest, morphometric data on blood vessels involved in CABG surgery is limited in South Africa which poses an immediate challenge for clinicians considering ways to improve postoperative outcomes.

1.5 RESEARCH AIMS

The aim of the study was to investigate which of the conduits used as grafts for CABG surgery are morphologically and histologically compatible to coronary arteries; a survey was also used to account for the objective factors that affect suitability. Comparative analysis on the morphometric data was conducted with the intention to rank them based on similarity in terms of length, diameter, and arterial wall thickness. These similarities imply that the conduits would have made a patent, functional, and durable graft (Tinica et al., 2018).

In achieving the aim, the following objectives were met:

1.5.1. Analysis of angiographic data of patients with CAD to ascertain the typical morphometry of healthy versus diseased coronary arteries. The angiograms were collected from a Groote Schuur Hospital, Cape Town in 2021.

1.5.2. Obtaining the length, luminal diameter, and wall thickness of the left coronary artery (LCA), right coronary artery (RCA), anterior interventricular coronary artery (AICA), posterior interventricular coronary artery (PICA), and the left circumflex artery (CX) to ascertain their standard morphometry, including their variations. The measurements were obtained from the angiograms (1.5.1.), and the cadavers from the University of Cape Town (UCT) in 2021.

1.5.3. Measurement of the length, luminal diameter, and wall thickness of the following conduits typically used as grafts in CABG: saphenous vein (SV), right and left internal thoracic artery (ITA), right gastroepiploic artery (RGEA), radial artery (RA), inferior epigastric artery (IEA). The measurements were obtained from the angiograms and the cadavers.

1.5.4. Comparison of the two data sets (coronary artery versus conduit) to ascertain, via a ranking system, which of the conduits in 1.5.3. are most similar to the coronary arteries in 1.5.2.

1.5.5. Conducting a qualitative survey of clinicians who engage in CABG surgery to ascertain the factors they consider the most when selecting a conduit that they deem an appropriate graft for CABG surgery.

CHAPTER 2: LITERATURE REVIEW

2.1. EMBRYOLOGY OF THE CVS

The cardiovascular system is the earliest system to emerge in the embryo during the period of the pre-somite stage (Conti, 2013). In the early phase of development, the embryo relies on simple diffusion of nutrients, oxygen and metabolic waste to survive, but with increased development structures become more complex and a circulatory system becomes necessary (Abdulla et al., 2004, Miller - Hance et al., 2012). The process of vasculogenesis begins with the differentiation of mesodermal cells into hemangioblasts and eventually into angioblasts [Figure 2.1]. When angioblasts form clusters they create "blood islands" which in turn become the precursor regions where vasculogenesis will occur (Moore and Persaud, 2004). The venous system arises first during vasculogenesis through the production of endothelial cells which play an important physiological role in angiogenesis, the physiological process for the development of blood vessels. Capillaries emerge from a monolayer of endothelial cells being laid due to angiogenesis (Sagar, 2019).

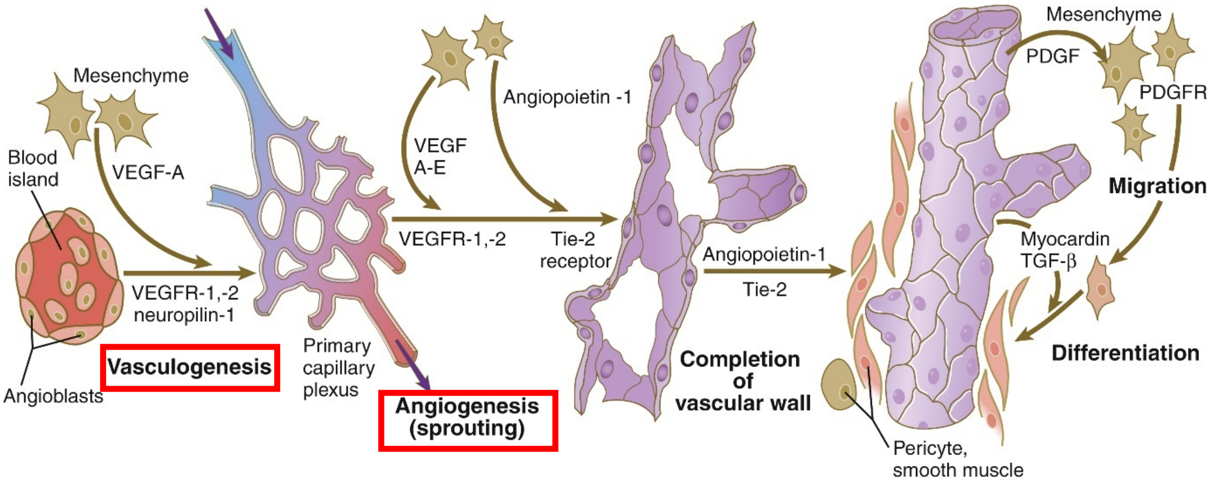


Figure 2.1: Early vascular development through the initial process of vasculogenesis and angiogenesis (Carlson and Kantaputra, 2019).

Angiogenesis differs from vasculogenesis since it requires existing blood vessels (containing endothelial cells) to develop the vascular network. Endothelial cells play a role in arterial remodelling even during adult life (Yang et al., 2018). The CVS is mainly a derivative of the mesodermal germ layer of cells which differentiates into myocardium, endothelium and mesothelium. Myocardial cells will develop into cardiac muscle (Carlson and Kantaputra, 2019). Endothelium will continue to form the blood vessels, lymphatics and endocardium which is the inner layer of the heart. The mesothelium will form the pericardium which is the outer layer of the heart (Crescent, 2017).

The development of the heart begins from primitive heart tubes that stretch, fuse and eventually fold resulting in the formation of a primitive heart that closely resembles the adult heart and its chambers (Moore and Persaud, 2004). The heart will then undergo a process called septation due to precursor structures called endocardial cushions that will develop into valves of the heart later in development (Abdulla et al., 2004, Person et al., 2005) [Figure 2.2].

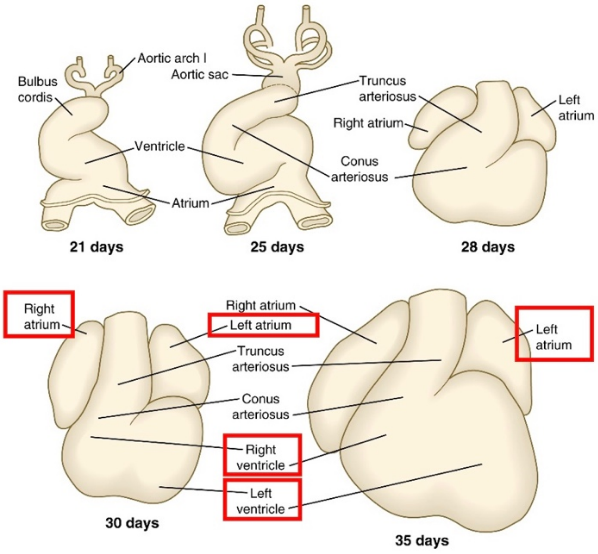


Figure 2.2: Development of the heart after early vasculogenesis and angiogenesis up until the septation forming the four chambers of the heart (Carlson and Kantaputra, 2019).

Anomalies can occur during the embryological development of the cardiovascular system either due to genetic predisposition or imbalances in the physiological environment to which the foetus was exposed (Crescent, 2017). These congenital anomalies vary and often require immediate intervention at birth (Keogh, 2005, Lane et al., 2002) Conversely, lifestyle behaviours can result in an individual acquiring CVD. For example, poor diets, substance abuse and sedentary lifestyles are known to pose a risk for cardiovascular disease (Hu, 2009). Acquired CVD tends to be slow and progressive in nature. The extent that an acquired CVD poses risk for mortality often relates to its location. CVD in the distal extremities tends to result less often in fatality than when occurring in the appendicular system, i.e. strokes and heart attacks are more fatal than arterial blockages in the legs and arms (Bauersachs et al., 2019).

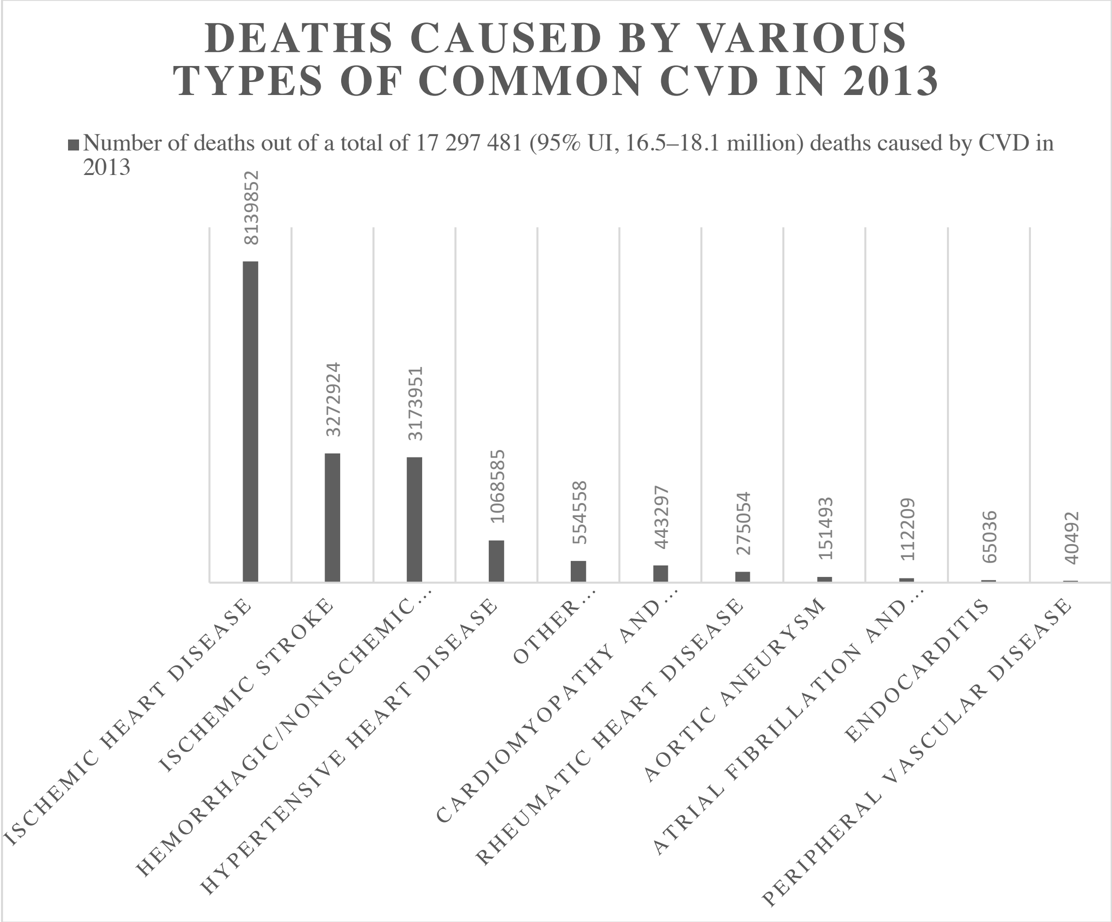
2.2. CARDIOVASCULAR DISEASE

Cardiovascular diseases are a global burden, specifically the types that are acquired. They can be divided into Coronary Heart Disease or Coronary Artery Disease (CAD) as well as Peripheral Artery Disease (PAD). These pathologies are characterized by the partial or complete occlusion of the vasculature leading to tissues supplied by the vessel in question becoming ischemic. There are other types of pathologies that can affect venous drainage normally due to a deterioration of venous valves, however, these have a lower mortality rate compared to pathologies of the arteries (White, 2003, Blann and Lip, 2006).

The location of an arterial pathology on the CVS can influence the likelihood of morbidity and mortality. For instance, a pathology in the blood supply of the head and neck i.e. cerebrovascular or carotid arterial disease could have more consequences than one occurring in the lower or upper limbs (Roth et al., 2015). Albeit, CAD is one of the leading causes of mortality in contrast to most cardiovascular diseases [Table 1].

Ischemic heart disease (IHC) is also referred to as CAD and it accounts for almost half of CVD related deaths, making it a leading cause of mortality. Its clinical manifestation is myocardial infarction or ischemic cardiomyopathy. Most individuals that have non-fatal CAD may have other comorbidities that put them at risk for disability, decreased quality of life, or death (Khan et al., 2020). Physical inactivity, stress, smoking, high blood cholesterol and diabetes are amongst the many risk factors for CAD (Bauersachs et al., 2019). CAD is traditionally considered a major burden in developed countries. This can be attributed to the general lifestyle of the population.

Table 1: The number of deaths caused by different types of CVDs globally during the year 2013 (Roth et al., 2015)



2.2.1. THE EPIDEMIOLOGY OF CAD

The prevalence of CAD is no longer exclusive to first world countries, and the trend can be observed in most developing countries (Abdelatif et al., 2021). Morbidities and mortalities in Africa and the Middle East are primarily caused by communicable, nutritional, and neonatal diseases. However, CAD is the next largest cause of death compared to all the former diseases combined, accounting for more than three-tenths of deaths (Yuyun et al., 2020). Whilst first world countries in Western Europe and North America tend to have higher numbers of CAD incidence; in the Sub-Saharan Africa (SSA) there tends to be fewer individuals aware of their diagnosis and even those who know are not on treatment (Carlson et al., 2017, Kakou-Guikahue et al., 2016).

Lifestyle behaviours associated with affluent societies are not the only set of risk factors for non-fatal CAD. Communicable diseases can also be a risk factor. Some investigations have shown that individuals living with HIV (ILWH) are at risk for the progression of CAD due to chronic HIV-related inflammation (Patel and Budoff, 2021). Although the mechanism is not clearly understood, ILWH are exposed to more risk of CAD the longer they live (Lacson et al., 2017). This fact can be attributed to the mechanism of CAD at a histological level, including its progressive nature.

2.2.2. THE AETIOLOGY AND TREATMENT OF CAD

CAD is primarily caused by atherosclerosis which is a pathology that affects histological layers of the coronary arteries of the heart. The slow and progressive nature of atherosclerosis encourages the infiltration of fatty cells which create plaque and that leads to the occlusion of the coronary arteries (Gustafson, 2010).

2.2.2.1. PATHOPHYSIOLOGY OF ATHEROSCLEROSIS

The endothelium provides the biggest endocrine function in the body. Its main functions include: immunology, inflammation, and angiogenesis (Félétou, 2011). The normal functioning of the endothelium is a key component of vascular health and when a disruption occurs, biochemical pathways are initiated as a response (Kharbanda and Deanfield, 2001). These responses may lead to changes in blood viscosity, platelet aggregation, and vascular remodelling.

Low-density lipoprotein (LDL) cholesterol, is a fat that circulates in the blood, moving cholesterol around the body to where it is needed for cell repair and depositing it inside of artery walls. Because cholesterol and triglycerides are insoluble in water, they must be associated with proteins to flow through the hydrophilic blood (Pirahanchi et al., 2021). Disrupted endothelium is at risk of being permeated by high concentration LDL (Doran et al., 2008). When LDL is oxidized it attracts leukocytes that impact the histological make-up of the TI. The inception of atherosclerosis is a complex interaction of processes that occur between the endothelium and blood via activated molecular messengers (Libby and Theroux, 2005) [Figure 2.3].

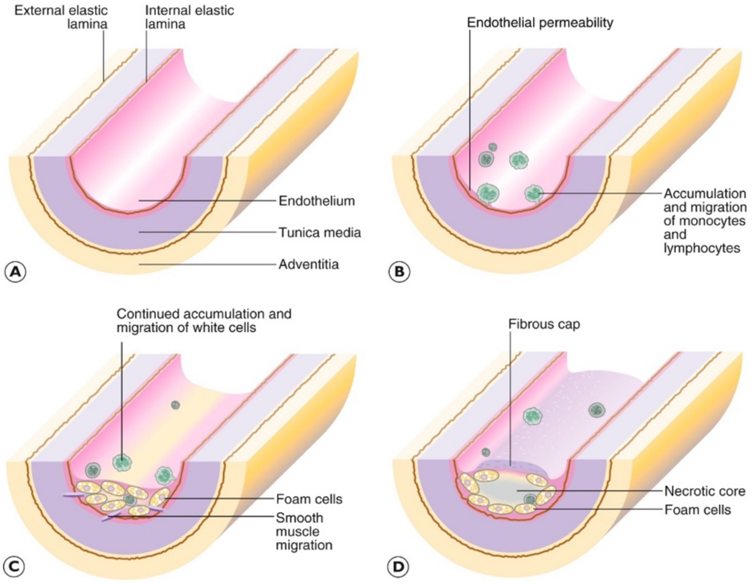


Figure 2.3: A) Healthy vasculature, B) immunological response due to endothelium dysfunction, C) accumulation of white cells, infiltration of low-density lipoproteins, and smooth muscle cell migration (vascular remodelling), D) the formation of plaque due to a fibrous cap, necrotic core and foam cells (O'Dowd et al., 2020).

In the early stages, atherosclerosis can be characterized by the formation of foam cells, fatty streaks and lesions in the TI (Gustafson, 2010). The lesions trigger signals that encourage smooth muscle cells (SMC) to infiltrate the fatty streaks [Figure 2.3]. When SMC are in the location of the fatty streak, they in turn encourage proliferation of white cells and extracellular matrix enters the lesion site. This process leads to the development of atherosclerotic plaque (Doran et al., 2008). When the plaque increases in size it begins to encroach on the lumen of the artery, decreasing the flow of blood to the tissue it supplies. This can have detrimental effects on the vascular health of the heart when occurring in the coronary arteries (Herrington et al., 2016).

2.2.2.2. TREATMENT OF CAD

When CAD is left untreated it can result in myocardial infarction. There are many interventions that clinicians can take to halt or even reverse the effects of atherosclerosis in coronary arteries. In individuals with early or non-fatal CAD, exercise, dietary changes, and pharmaceuticals can assist in regaining vascular health (Jaffer and Blankstein, 2021). However, in mild to severe cases interventions like percutaneous coronary intervention (PCI) and CABG tend to yield better results (Stone et al., 2019). Given the life-threatening nature of CAD, the correct selection and implementation of treatments is a direct determinant of the cardiovascular health of the affected individuals. CABG is considered the best treatment for mild to severe CAD since it can drastically improve the quality of life (Bakaeen, 2017).

Success of CABG surgery is characterized by the revascularization of the affected area and the patency of the conduit used as a graft. The survival rate of patients following CABG has increased in recent years, and this can be attributed to advances in surgical procedures, pharmaceuticals, and other multi-disciplinary interventions (Bakaeen, 2017).

2.2.3. THE HISTORY AND EVOLUTION OF CABG SURGERY

The first successful CABG surgery was reported by Dr G. Favaloro using the great saphenous vein (SV) as a graft (López-de la Cruz and Fleites, 2020, Favaloro et al., 1970) This was not the only attempt made between 1960 and 1970; others were reporting the use of the right or left internal thoracic (mammary) artery (ITA) as grafts. Early case reports not only illustrate the importance of graft selection but also surgical techniques like suturing, stapling, and the use of tantalum rings (Rocha, 2017). These clinical operations were deemed successful based on patient survival, the patency of the graft used, and symptom alleviation.

The SV used to be the most preferred graft due to its length, diameter, and its accessibility. However, concerns grew about its permeability being compromised due to adaptive histological changes like intimal hyperplasia (abnormal cellular changes) and atherosclerosis (Martínez-González *et al.*, 2017). Most literature supports the notion of arteries being superior to veins for grafting (Gaudino et al., 2018), whilst some argue that vessels like the SV can be superior to vessels like the radial artery, and as patent as the ITA if the “no-touch” technique is used during the harvesting of the graft (Dashwood and Loesch, 2019). The “no-touch” technique refers to the removal of a conduit vessel with most of its surrounding tissue (pedicle) intact to avoid vascular damage or trauma (Kopjar and Dashwood, 2016). The no-touch harvest method is known to preserve histological integrity since it minimizes perioperative damage during handling [Figure 2.4].

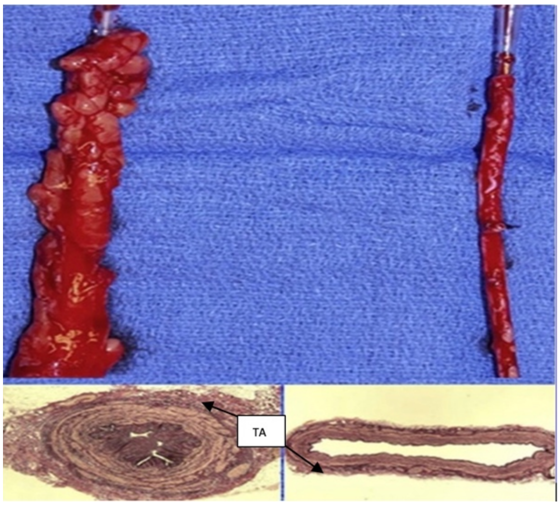


Figure 2.4: Two saphenous vein grafts and their corresponding histological images directly below each vein. The image on the left was harnessed via “no-touch” technique and consequently its histological integrity is maintained as opposed to the graft on the right. The TA is lost on the image to the right (Dashwood and Loesch, 2019)

2.2.3.1. CABG SURGERY IN CONTEMPORARY PRACTICE

The evolution of surgical techniques has been further aided by advances in biomedical engineering which have introduced machinery like the cardiopulmonary bypass machine (CPB). This means that CABG surgery can be conducted “on-pump”, which refers to the heart being stopped with the aid of a CPB, allowing for better handling and suturing of the coronary arteries (Fetrow and Dickerson). Although, there are some concerns pertaining to the use of the on-pump technique especially in patients with certain comorbidities (Jiang et al., 2022). There is no unanimity regarding the use of CPB as there is little or no evidence that the use or lack thereof has any impact on outcomes, on condition that the grafts are appropriately selected and sutured.

Suturing is a crucial part of CABG surgery since a good suture will result in good anastomosis. There are two broad categories for suturing; they are either sequential [Figure 2.5a] or continuous. Sequential anastomotic technique allows for greater use of conduit length, may improve graft patency, and allow for more complete revascularization with a better economy of conduit utilization (Schwann et al., 2017, Lee et al., 2016).

Most commonly used is continuous suturing which is a similar type of suture used for wounds. Another common type of suturing in CABG is aortic anastomoses which is not preferred by some clinicians due to the likelihood of aortic aneurysm formations postoperatively resulting from the manipulation of the aorta (Saha et al., 2011). The location of a conduit is very important when considering its suitability. A conduit that is closer to the affected coronary artery makes it appropriate since it requires minimal manipulation (Martínez-González et al., 2017) [Figure 2.5].

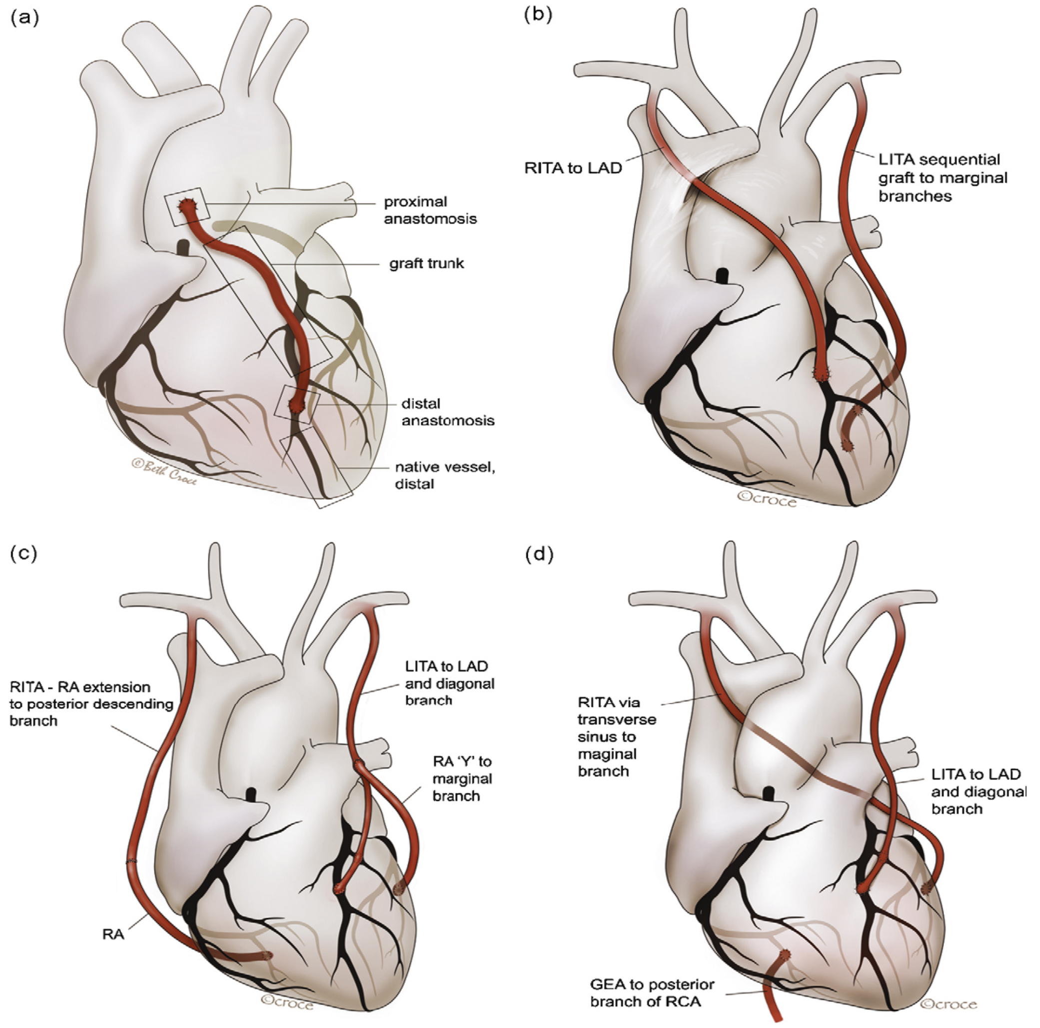


Figure 2.5: Images showing the types of anastomotic techniques used in CABG surgery (a) proximal (aortic), (b) & (d) distal, (c) sequential (Buxton et al., 2009)

2.2.4. CONDUITS SELECTION FOR CABG SURGERY

There are many standard practices adopted worldwide for CABG surgery, although the question of which conduit is superior for achieving long-term myocardial revascularization still persists (Gaudino et al., 2018). This can be attributed to the multifactorial nature of CAD in patients and the array of characteristics that make a graft ideal. Arteries most frequently affected by CAD are the right coronary artery (RCA), anterior interventricular coronary artery (AICA) and the circumflex artery (CA) (Mtz et al., 2015).

When applying the core principle, that a graft should be morphologically similar to the affected coronary artery, certain parameters must be considered when determining the graft's suitability. These parameters are length, luminal diameter, wall thickness and histological characteristics (Bakaeen et al., 2013, Martínez-González et al., 2017). Literature based evidence is the most prevalent factor affecting conduit selection by a surgeon, second to it is the consultant or surgeon's experience (Jayakumar et al., 2019).

2.2.4.1. CORONARY ARTERIES

Not all coronary arteries have the same morphology, therefore, susceptibility to pathology is different. The AICA, CX, and RCA tend to have a higher incidence of CAD (Rösch and Rahimtoola, 1977). Literature also shows that the principle of flow disturbance due to hemodynamic flow at bifurcations also applies to coronary arteries (Ghista and Kabinejadian, 2013). Knowledge about typical location of atheromas is not conclusive (Martínez-González et al., 2017). The location and magnitude of the occlusion is an important consideration when selecting a graft, since severe occlusions could mean the procedure is done under acute conditions (He, 2006). Some studies have explored parameters such as the length of the coronary arteries, which are population variations (ÜnlÜ et al., 2003) [Table 2]. Although the luminal diameter is frequently investigated and the mean dimensions are often inconsistent from study to study. A better understanding on the morphology of the coronary arteries is crucial since it is the premise that determines a graft's suitability.

Table 2: Morphological studies on the coronary artery

Author (year)	Country	Sample Size	Coronary Artery	Mean length (cm) ± standard deviation
ÜnlÜ et al. (2003)	Turkey	29 bodies	AICA	9.38 ± 1.84
			RCA	6.60 ± 1.53
			CX	5.70 ± 1.20
Martinez-Gonzalez et al. (2017)	Mexico	10 bodies	AICA	15.66 ± 1.12
			RCA	12.69 ± 1.94
			CX	8.89 ± 2.11

2.2.4.2. STUDIES ON THE INTERNAL THORACIC ARTERY

The novel use of an ITA graft, in CABG, was conduct by Vineberg (1946). In modern practice, both the right and left ITA are considered the most preferred for grafting due to morphological characteristics that make it is less prone to developing atherosclerosis and intimal hyperplasia. Intimal hyperplasia refers to an aggressive cell proliferation in the intima which may result in endothelial dysfunction and consequently vascular remodelling (Yang et al., 2018). The ITA, as a muscular artery, is also favoured due to its permeability and the histological features which closely resemble coronary arteries. There is a greater preference for the left ITA due to its proximity to the heart, allowing for easier surgical access and manipulation during anastomosis (Taggart et al., 2016, Weiss et al., 2013, Berdajs and Turina, 2011). The use of left ITA (LITA) to re-establish circulation to the AICA is the known as the best practice (González Santos et al., 2005). The right ITA (RITA) is useful for revascularizing branches of the LCA or branches of the LCX. However, since it remains attached to the subclavian artery, the verification of its permeability is difficult. As a result of this, it is more suitable for bypassing the RCA, or in instances where it's length is appropriate, the PICA (González Santos et al., 2005).

Literature shows that neither ITA has a consistent histological make up along its length, hence it is known as a transitional artery (Kneubil et al., 2006, Labudović Borović et al., 2010). The histological inconsistency has casted some doubts about its patency when grafted onto coronary arteries (Kinoshita et al., 2014). There are studies that show differences between the LITA and RITA, while some report similarities in their histological structures (Kinoshita et al., 2014). These vessels have a reported length ranging from 14.32 to 19.48 cm. Henriquez-Pino et al.(1997) demonstrated that difference in length of both ITAs was negligible, the mean difference is 0.6 cm. Morphological studies of the ITA, whereby the diameter and the wall thickness were investigated, are shown in Table 3 below. The diameter tends to vary along the segments of ITA. Proximally it has been reported to range between 2.12 to 2.75 mm and 1.03 mm to 1.75 mm distally (ÜnlÜ et al., 2003).

Studies comparing the RITA and LITA have reported a mean of 1.72 mm and 1.76 mm, respectively (Appleson and Hill, 2012). In studies in which segments were generalized, the luminal diameter ranged between 1.6 and 2.75 mm (Hinojosa Amaya et al., 2010). In similar studies, a wall thickness of 350 µm is reported (González Santos et al., 2005, Hinojosa Amaya et al., 2010). Histologically, the ITA is has the characteristics of both a muscular and elastic artery (Labudović Borović et al., 2010) which has been used to justify its long-term patency, as it is mentioned that the more elastic the graft is, the greater its permeability will be over time (He, 2006). The TI is thin, and the TM is barriered by a well-defined IEL. There are two layers in the TM: one found internally and another externally (Labudović Borović et al., 2010). The internal layer is muscular, composed mainly of SMC with few elastic fibres that are not well formed. The external layer is elastic, composed mainly of well-defined elastic fibres with few muscle cells (Labudović Borović et al., 2010). The compact structure of the IEL has been attributed to the low occurrence of intimal hyperplasia in the ITA.

Table 3: Morphological studies of the internal thoracic arteries

Author	Country	Sample size	Luminal diameter (mm) ± standard deviation	Thickness of tunica media (µm) ± standard deviation
Barry et al. (2007)	France	40 bodies	1.6 ± 0.3	218.3–257.7
ÜnlÜ et al. (2003)	Turkey	29 bodies	2.12 ± 0.27	253 ± 43
Kinoshita et al. (2014)	Japan	72 patients	$m = 1.60$	$m = 172$
Appleson and Hill (2012)	USA	7 bodies	$m = 1.72$	$m = 0.22$

2.2.4.3. STUDIES ON THE RADIAL AND ULNAR ARTERY

The radial artery (RA) was the first artery used in 1973 for CABG (Baikoussis et al., 2014). The RA is considered the second most used vascular conduit in general due to its suitable thickness, luminal diameter, and length (Barner, 2013). Its length and thickness make it easy to handle and anastomose; it also has a morphology similar to coronary arteries (Carpentier et al., 1973, Baikoussis et al., 2014). Other factors that contribute to its suitability is its adaptability to changes in blood pressure and its permeability, although it has been known to be prone to vasospasms (Hinojosa Amaya et al., 2010). The vasospasms are caused by an increased number of smooth muscle cells within the tunica media (TM). However, there are harvesting techniques and pharmaceutical drugs (González Santos et al., 2005) that assist in averting vasospasms. Should vasospasms occur, they may lead to potentially fatal myocardial infarctions (Gaudino et al., 2019). Additionally, the prevalence of intimal hyperplasia and atherosclerosis is more common in the RA than in the ITA. Hyperplastic changes also contribute calcification in the tunica media (Monckeberg's Sclerosis) with a prevalence of 25% (Chowdhury et al., 2004). The RA is usually anastomosed with the RCA, CX, or PICA and its use as a conduit in these vessels has been associated with satisfactory clinical and angiographic results. In other instances, which tend to be rare, the RA is used to anastomose the AICA (Hinojosa Amaya et al., 2010).

Complications after the extraction of the RA are rare when adequate preoperative assessments and precautions are performed (Henriquez-Pino et al., 1997, Hinojosa Amaya et al., 2010). Common complication arising from poor resection of the RA are neurosensory complications in the posterolateral aspect of the upper limb. These neurosensory complications rarely manifest as debilitating symptoms, such as persistent tingling or neuromotor dysfunction in the forearm and wrist.

The occurrence of sensory dysfunction usually disappears shortly after harvesting (González Santos et al., 2005). After grafting the RA in CABG, it undergoes functional and morphological remodelling characterized by increased luminal diameter and decreased SMC thickness. It is reported that the main cause of graft failure is vasospasms or hyperplasia (Chowdhury et al., 2004). Results of various morphological studies of the RA, where the length, luminal diameter, and thickness of the tunica intima and media are determined, are shown in Table 4. In instances where the RA is difficult to obtain, the ulnar artery (UA) is used as an alternative although more work needs to be done to investigate its patency (Goldman et al., 2011, Martínez-González et al., 2017).

Table 4: Morphological studies of the radial artery

Author	Country	Sample size	Length (cm) ± standard deviation	Diameter (mm) ± standard deviation	Tunica media (µm) ± standard deviation
ÜnlÜ et al. (2003)	Turkey	29 bodies	22.28 ± 3.31	3.2 ± 0.5	321 ± 32
Hernández et al. (2013)	México	10 bodies	21.94 ± 3.34	1.48 ± 0.70	196.16 ± 72.35
Nasr (2012)	Egypt	50 bodies	22.6 - 21.7	3.3 ± 0.72	

Hinojosa Amaya et al (2010), drawing on the study by Buxton et al (1998) reported the first use of the UA, stated that the use of UA as a graft is not popular, with the RA being preferred. The removal of the UA, being the dominant artery in the forearm, may result in functional disorders of the hand (Newcomb et al., 2006). However, it has been used in surgical procedures of myocardial revascularization surgery and reconstruction (Hinojosa Amaya et al., 2010).

2.2.4.4. STUDIES ON THE RIGHT GASTROEPIPLOIC ARTERY AND THE SAPHENOUS VEIN

The right gastroepiploic artery (RGEA) is considered the third best option, with some authors considering it equivalent to using the SV when it is not harvested using the "no-touch" technique. It is a very versatile conduit, it provides 20 cm in length, and is capable of reaching all the areas of the heart (González Santos et al., 2005). Similar to the internal thoracic artery, the RGEA can be grafted *in-situ*. This means that it can remain attached on one end which allows for easier manipulation and increased patency (Suma, 2016). However, there are some concerns in its use: its small size and its propensity to vasospasm (Van Phung et al., 2012). The RGEA is mainly used for revascularization of the inferior aspect of the heart, particularly the PICA (González Santos et al., 2005). It is also used in the distal segment of the RCA. In most patients, RGEA is used in conjunction with the left ITA and the RA in an attempt to achieve complete revascularization of different coronary vessels (González Santos et al., 2005, Pym, 2006). More commonly, the RGEA is used as a free graft and can revascularize more than one artery by one or more side anastomosis (González Santos et al., 2005). The anastomosis with the AICA has poor results, although, abdominal complications due to extraction of the RGEA are rare (Malvindi et al., 2007) [Table 5].

Table 5: Morphological studies on the RGEA

Author	Country	Sample size	Mean length (cm)	Diameter (mm)	Tunica media (µm)
Kneubil et al. (2006)	Turkey	29 bodies	19.32–20	2.5-2.7	274
ÜnlÜ et al. (2003)	Brazil	18 bodies	20-21	1.8-3.8	305

There is considerable debate as to the suitability of the SV relative to the RGEA and the RA (Loesch et al., 2019). This is due to the SV's long-standing use in CABG (Favaloro et al., 1970). Concerns are based on the fact that a vein cannot graft onto an artery due to differences in histology. This difference is the main reason used to justify why veins do not surpass the 10-year postoperative mark of arteries (Caliskan et al., 2020).

2.2.4.5. THE INFERIOR EPIGASTRIC ARTERY

In some cases where it is difficult to use these more favourable conduits, the inferior epigastric artery is used in CABG (Martínez-González et al., 2017, Barry et al., 2007) Some patients may not be considered suitable for a bilateral ITA graft due to comorbidities like pulmonary disease. The IEA becomes useful in those instances (Buche et al., 1992).

2.3. CONCLUSION

When conduits are selected for CABG surgery there can be disadvantages present which may be subjectively based on a patient's circumstances or factors such as the morphology of the graft itself. Furthermore, literature shows that most atheromas occupy proximal segments of coronary arteries which may be due to the decreasing diameter of the vessel as it courses distally, in a conical-like manner (Gaudino *et al.*, 2018). Human variation is another factor that can affect a clinician's decision of which conduit is most suitable (Loukas *et al.*, 2013). The exact preferability of one vascular conduit to another had not been fully ascertained in earlier years although in contemporary reviews, some generalized consensus has been established as to which conduits are more suitable (Martínez-González et al., 2017, Barner, 2013) [See Table 6 below].

Gaps exist in literature pertaining to the distinct definition of the morphological characteristics that make conduits suitable grafts i.e., vessels ranging from *x* diameter or length, or vessels that have a TI or TM of *x* thickness are more suitable. Furthermore, there are no morphometric studies in South Africa indicating conduit suitability. Hence, investigating the suitability of conduits from a morphometric standpoint, can give South African clinicians guidance regarding the suitability of grafts based on their similarity to coronary arteries.

Table 6: Rankings from review articles in the last decade of conduits most used to the least, the pros and cons for each conduit, and quantitative data sorted according to parameters set out in the review studies

Review title and author	Ranked according to preference	Pros	Cons	Length (cm)	Diameter (mm)
1.Conduits for Coronary Bypass: Arteries Other than the Internal Thoracic Artery's. (Barner, 2013)	1.Radial artery	Relatively consistent length and diameter > ITA.	Vasospasms due to muscular cells that may reduce patency.	20-24 (2cm less in females)	2.5
	2.Right gastroepiploic artery	Better > RA as a free graft = better routing.	Smaller and usually more fragile.	-	-
	3.Inferior epigastric artery	Bilateral structure that is possible to harvest without entering the body cavity.	Reports of abdominal wall necrosis in 2 out 17 patients after harvesting.	-	-
2.Conduits Used in Coronary Artery Bypass Grafting: A Review of Morphological Studies. (Martínez-González et al., 2017)	1.Internal thoracic artery	Long term patency, best permeability and reduced operative risk.	Transitional TM i.e. contains some SMC and elastic fibres.	14.32 - 19.48	2.12 - 2.75 proximally, 1.03 - 1.75 distally
	2.Radial artery (or Ulnar artery when the RA is not accessible however it not preferred).	Vast length and thickness that makes it easier to handle and anastomose.	A thick TM means more SMC and consequently vasospasms.	females 20.9 ± 13.9 males 22.6 ± 21.7	3.3 ± 0.72 proximally, 3.0 ± 0.72 distally
	3.Right gastroepiploic artery	Versatile and can reach most areas of the heart.	Fragile and small with a propensity to get spasms.	19.32–20	3.3 ± 0.72 proximally, 3.1 ± 0.73 distally
	4.Inferior epigastric artery	-	-	-	2.5 to 2.7 proximally, 1.8–3.8 distally

CHAPTER 3: METHODS AND MATERIALS

3.1. STUDY DESIGN

The investigation had a quantitative, cross-sectional, and observational design. It was retrospective in nature. Samples were obtained from coronary angiograms and cadaveric bodies. A survey was also conducted between dates 24 August 2022 to 22 September 2022. Non-probability sampling methods were used for all components of the study. The non-probability sampling methods were limited to convenience and purposive sampling.

3.2. SETTING

i. Coronary angiograms

Coronary angiograms from 109 individuals were collected from the Department of Cardiothoracic Surgery at Groote Schuur Hospital (GSH). Data was collected between September 2021 – November 2021.

ii. Body cohort

Bodies donated to the University of Cape Town's (UCT) Department of Human Biology, for the year 2021, made up the body cohort for this study. Body dissection and histological analysis was conducted between August 2021-December 2021.

iii. Survey

A survey was distributed amongst members of the Society of Cardiothoracic Surgeons South Africa (SCTSSA) (Appendix 1). The survey was designed on Limesurvey® using questions that were adapted from a study conducted in Europe (Jayakumar et al., 2019). The survey was first sent out on the 24th of August 2022. An initial 14 day period was open for responses; with a further extension of 14 days granted. Reminders were sent out at least twice during the 28 day period.

3.3. SUBJECTS

i. Coronary angiograms:

The inclusion criteria for the angiograms were limited to adults with images of all five coronary arteries (RCA, LCA, LCX, AICA and PICA) clearly visible. The exclusion criteria included individuals with missing meta data such as age and sex. Images that were distorted or had coronary arteries that are not clearly contrasted were also excluded.

ii. Body cohort:

The inclusion criteria for the bodies included cadavers that had some coronary arteries (RCA, LCA, LCX, AICA and PICA) and vascular conduits (LITA, RITA, RGEA, SV, RA, IEA) available. The exclusion criteria were based on the availability of the coronary arteries; bodies with less than 3 coronary arteries due to damage due to prior teaching and learning were excluded. The entire vessel was resected.

iii. Survey:

The inclusion criteria for the survey responses were limited to cardiothoracic surgeons; from junior registrars to consultants. Responses that were not completed from the first section until the last were excluded.

3.4. ETHICAL APPROVAL

Ethical approval was granted by the Faculty of Health Sciences Human Research Ethics Committee at the University of Cape Town (HREC REF: 483/2021) (Appendix 2). Furthermore, approval was granted by GSH to access patient data in a manner consistent with the Western Cape Government's health policies.

3.5. DATA MANAGEMENT PLAN

i. Coronary angiograms

The coronary angiograms obtained from the Cardiothoracic Clinic were transferred onto an external hard drive which was only accessed by the Primary Investigator (PI). Basic demographic data was recorded in an Excel spreadsheet that included meta data, for example, age and sex. The coronary angiograms will be retained for a period of 1 year after the study is concluded. Thereafter, the coronary angiograms will be deleted. The Excel spreadsheet, containing no patient details, is stored on a secure Google Drive shared only between the PI and supervisors.

ii. Body cohort

All measurements and demographic data from the bodies were recorded directly onto an Excel spreadsheet which is stored on a secure Google Drive shared only between the PI and supervisors.

iii. Survey

The survey was sent from the PI's UCT email to the Secretary of SCTSSA for dissemination. The email included a summary of the study and a link to Limesurvey®. All responses, which included participant names, were stored on a private Google Drive that is only shared between the PI and supervisors.

3.6. SAMPLE SIZE

A one-way ANOVA power analysis was conducted for both the coronary angiogram and the body cohort samples using SPSS. The sample sizes were 105 and 40 for the coronary angiograms and the body cohort, respectively. The coronary angiogram samples had an observed power value of 0.83

which was computed using alpha. The body cohort had a observed power value of 0.51 which was also computed using alpha (Appendix 3). Therefore, the probability for Type II error is 0.12 and 0.49 for the coronary angiogram and body cohort samples, respectively.

3.7. RELIABILITY

All measurements were repeated three times and the average value out of the three was considered as the most accurate. The vessels obtained from the bodies were measured in-situ and also after resection.

An experienced radiologist from GSH observed randomly selected coronary angiograms (N=22) to confirm whether the interpretation of the images was done correctly. The radiologist conducted measurements on them using the same software and computer, and the values that were obtained were put through a reliability test on SPSS.

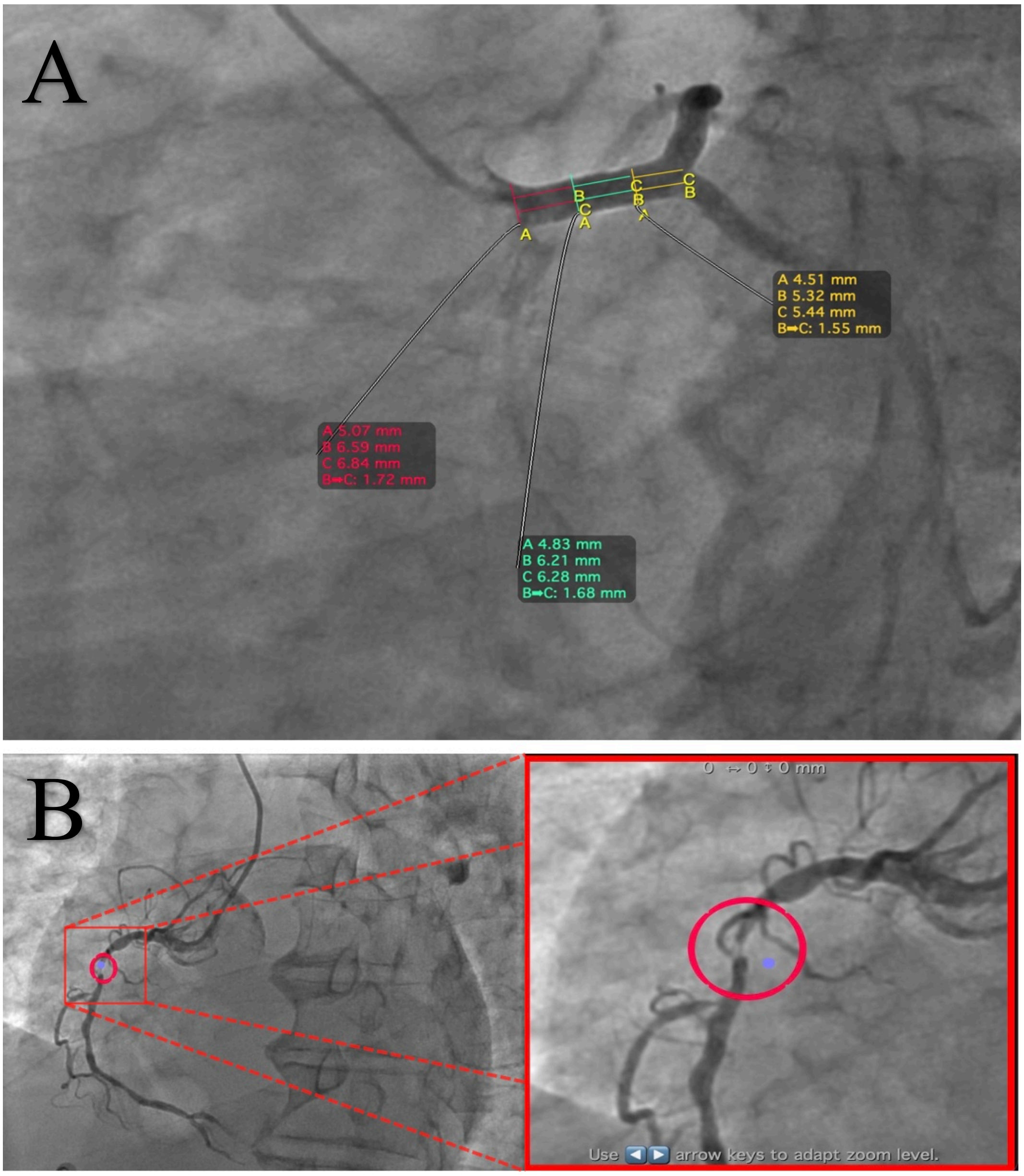
Clinical Anatomy Masters students from the Human Biology Department conducted repeated measurements on the resected vessels obtained from the bodies using the same method and tools (Appendix 4).

3.8. METHODOLOGY

3.8.1. CORONARY ANGIOGRAMS

The metadata accompanying each angiogram included the c-arm rotational angles for each image which aided in orientating and identifying the coronary vessels, therefore images were measured at different angles. The patients' names were replaced with case numbers created by the PI, and loaded onto a DICOM viewer software called Orisix®. The coronary angiograms were sorted into two cohorts according to the diagnosis: individuals with CAD and individuals without CAD. A Robot Operating System (ROS) function built onto the DICOM viewer software was used to measure the diameter and lengths of coronary vessels.

In order to measure the diameter of the vessels, measurements were taken at 3 points on the artery: at the origin, midpoint, and terminal. A similar approach was done for the length at each segment. The average diameter and length was then calculated and recorded [see Figure 3.1 below].



Key

A: Diameter Measurement 1

B: Diameter Measurement 2

C: Diameter Measurement 3

Figure 3.1: (A) The diameter and length of the LCA measured using perpendicular lines on Ostrix software. (B) A left anterior oblique (30º) cranial view of an occluded RCA with a zoomed in image on the right.

In order to measure the length of the LCA and RCA, the ostium was the origin and the terminal part was at the bifurcation or at the tapering end for the LCA and RCA, respectively. The LCX, AICA, and PICA were measured from the point where it bifurcated to the tapering end [Figure 3.2].

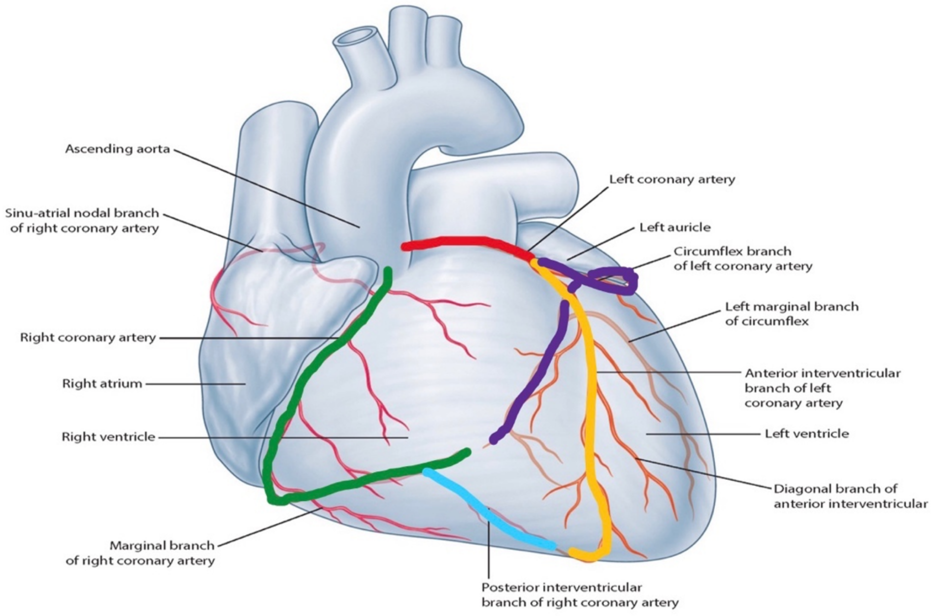


Figure 3.2: The RCA (green), LCA (red), LCX (purple), AICA (orange), and PICA (blue) were measured and resected at the origin and terminal points (Drake, 2015)

3.8.2. Body cohort

3.8.2.1. Dissection and measurement

The bodies were already dissected due to prior teaching and learning. The dissection was carried out using a standard student dissection kit, and the resection of the RCA, LCA, LCX, AICA, PICA, LITA, RITA, RA, RGEA, SV, and the IEA was done according to the protocols outlined in "Grants Dissector" (Tank and Grant, 2012). Each coronary artery was resected at its' origin to its termination at the bifurcation or the tapering end [Figure 3.2].

Conduits and coronary arteries obtained from the dissection were measured for their length from end-to-end on a measuring tape that was fixed against a table; and a digital calliper was used to obtain their diameters. Measurements were conducted three times both in situ and also after resection [Figure 3.3]. The average measurement was recorded.

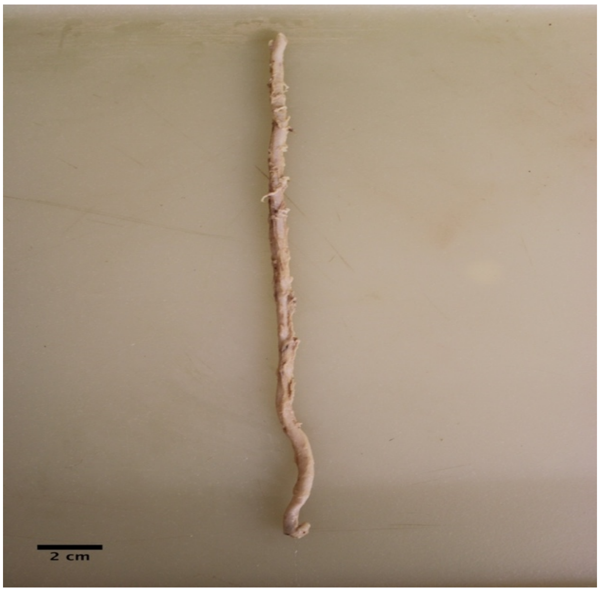


Figure 3.3: An image of a resected radial artery

3.9. HISTOLOGICAL SAMPLES

3.9.1. TISSUE PROCESSING

The resected vessels were left overnight in 10% formalin solution. Thereafter, the specimens were numbered and registered before processing. The Taylor and Bordoni (2019) tissue preparation protocol was followed. All processed resections of the coronary arteries were divided into two portions at the midline and labelled proximal and distal sections in order to account for various segments of the coronary artery (Figure 3.4). The other conduits were divided similarly at their "head-and-tail" ends, which are the points of contact during grafting.

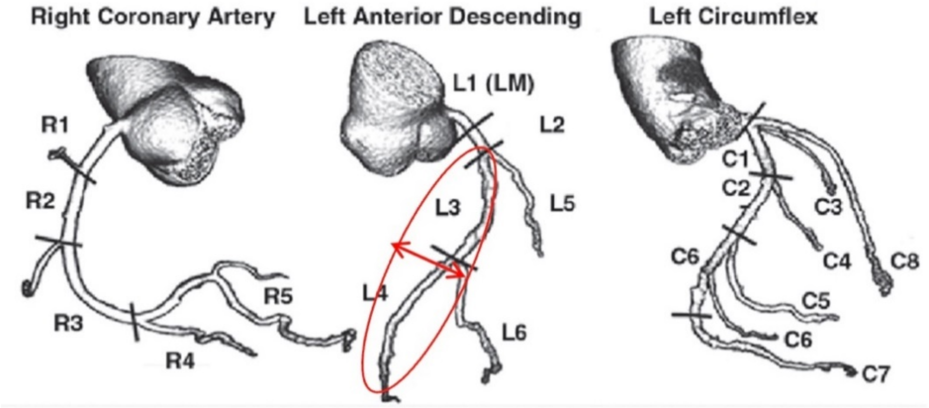


Figure 3.4: A cut (↕) in the midline of the left anterior descending (⬯) or AICA dividing its segments (L3 & L4) into proximal and distal portions.

The proximal and distal parts were carefully assigned a serial number, accounting for it’s source, in a sequential manner and entered into an Excel spreadsheet. The two portions obtained from each vessel were put into a cassette in a consistent manner (Figure 3.5).

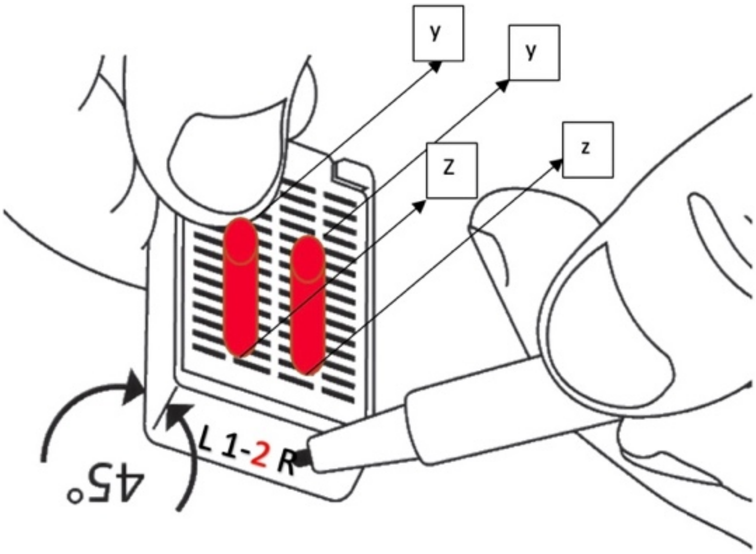


Figure 3.5. A tissue processing cassette landmarked into left (L) and right (R) border containing the first vessel divided sequentially into proximal (1) and distal (2) portions that are orientated with the midline (z) towards the 45º part of the cassette. The origin (proximal) and terminal (distal) ends of the vessels (y) are situated at the opposite end.

(Image adapted from: https://en.medpip.com/product/tissue-cassette-with-lid/)

Each body had 11 vessels (5 coronary and 6 vascular conduits) of interest, meaning that 40 bodies had an expected yield of 440 arteries to be used in individual cassettes, which were divided into two portions and labelled sequentially. The highest number in the sequence being 880. The vessels obtained were then put into a tissue cassette rank and then into the Leica TP 1020 automatic tissue processor according to a strict protocol (Figure 3.6).

Beaker	Solution	Time in solution (hr)	Setting on SE 400 processing machine
1	10% Buffered	1	0-1
2	Formalin 70%	1	1-2
3	Alcohol	1	2-3
4	70% Alcohol	1	3-4
5	90% Alcohol	2	2-3
6	90% Alcohol	2	4-6
7	Absolute Alcohol	2	6-8
8	Absolute Alcohol	2	8-10
9	Absolute Alcohol	2	10-12
10	Xylol	2	12-14
11	Xylol	2	14-16
12	Wax	2	16-18
13	Wax	4	18>

Figure 3.6: Tissue processing schedule for the Leica TP 1020 automatic tissue processor.

3.9.2. SECTIONING & STAINING

Tissue samples were placed in melted paraffin wax to facilitate histological sectioning after cooling. The embedded tissue was fixed on the block holder of a microtome for trimming and section cutting into 10µ slices. The sections were moved onto a slide, floated with 70% ethanol, and then transferred into a warm bath (~30°). Thereafter, the section was left to dry overnight, in preparation for de-waxing in Xylene and rehydration progressing through alcohols and water, respectively. The sections were then stained by the Haematoxylin-Eosin (H&E) stain which is commonly used for arterial wall staining. This makes the tunica intima and tunica media distinguishable.

3.10. STATISTICAL ANALYSIS

i. Coronary angiograms

The data obtained from the angiographic and body samples was analysed using descriptive quantitative statistics. The variables assessed were the vessel length (in mm), luminal diameter (in nm), and the intimal and medial thicknesses (in um). The raw measurements of all the morphometric dimensions obtained from these vessels was inserted on a *Microsoft Excel Spreadsheet* and subjected to statistical analysis to ascertain similarities or discrepancies between the coronary arteries of individuals with CAD with their corresponding vascular conduits. A Pearson correlation test was used instead of a t-test because the variables tested were continues or in other instances binary. Univariate and bivariate analysis were used for the descriptive statistics. These tests were used to test the hypothesis that the morphology of coronary arteries with CAD differs from samples without. The null hypothesis is that there is no correlation in the morphology between individuals with and those without.

ii. Body cohort

The microscopic images obtained from the proximal and distal regions of the coronary arteries made up the standard. These images were compared with the images obtained from the tail and head ends of the conduits. The histological wall thickness was measured using *Image J* software to ascertain the intimal and medial thickness associated with both sample groups and the sum of both (coronary arteries versus conduits). This was done with the use of the ROI feature, on *Image J*®, three parallel lines made from the TI to the TA and the average measurement of these three lines were considered. All histological images were captured at a magnification of 250x and a scale bar of 100 µm was used as reference [Figure 3.7].

iii. Survey

This involved descriptive statistics. The charts were made with Microsoft Excel Spreadsheet.

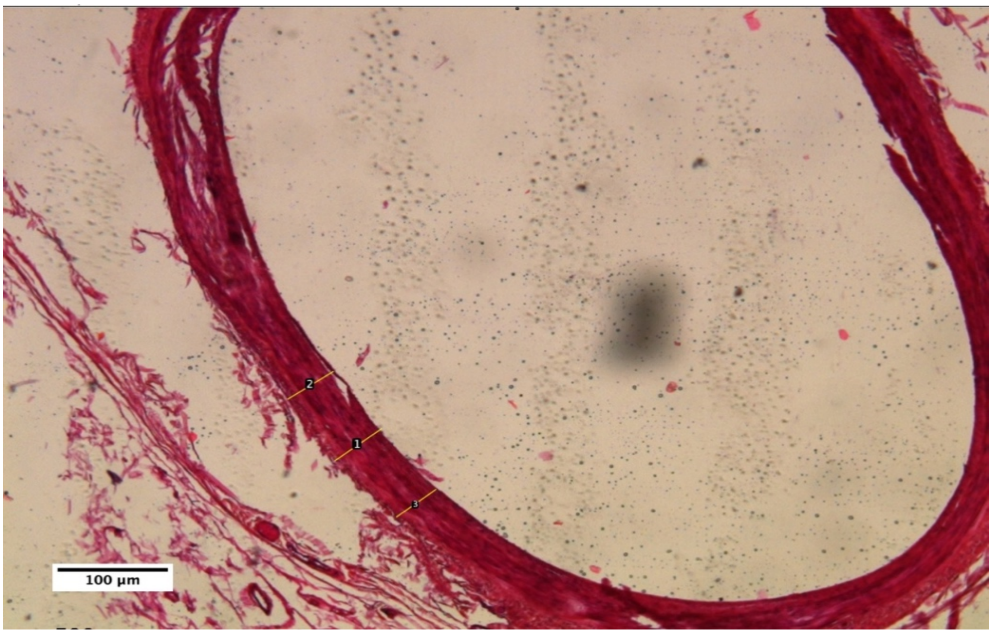


Figure 3.7: A H&E-stained section of an AICA, with a scale bar of 100 um (250x); yellow lines measuring the arterial wall thickness.

CHAPTER 4: RESULTS

The results will be presented in three parts. The first part will report on the coronary angiogram cohort, the second on the bodies, and the last will report on the survey. All parts will begin with an introduction that contains descriptive statistics such as sample size, sex and age distributions.

A reliability test was conducted on SPSS which resulted in a Cronbach's Alpha value of 0.99 which indicates strong intra-observer reliability. A Cohen's Kappa test resulted in a value of 0.92 which shows strong inter-observer reliability for the coronary angiograms. The data obtained from the body cohort was subjected to a Cohen's Kappa test and it resulted in a value of 0.91 indicating strong inter-observer reliability.

4.1. CORONARY ANGIOGRAM COHORT

4.1.1. DESCRIPTIVE STATISTICS

The coronary angiogram cohort consisted of 109 individuals, however, only 105 were deemed appropriate for morphometric analysis. A total of 4 bodies were excluded due to the coronary arteries being completely obliterated or unavailable. There were no excluded coronary arteries from the 105 individuals. Out of the 105 individuals; 37 were without CAD while the other 68 had CAD. This was identified by visible occlusions on at least one coronary artery [Figure 4.1.1].

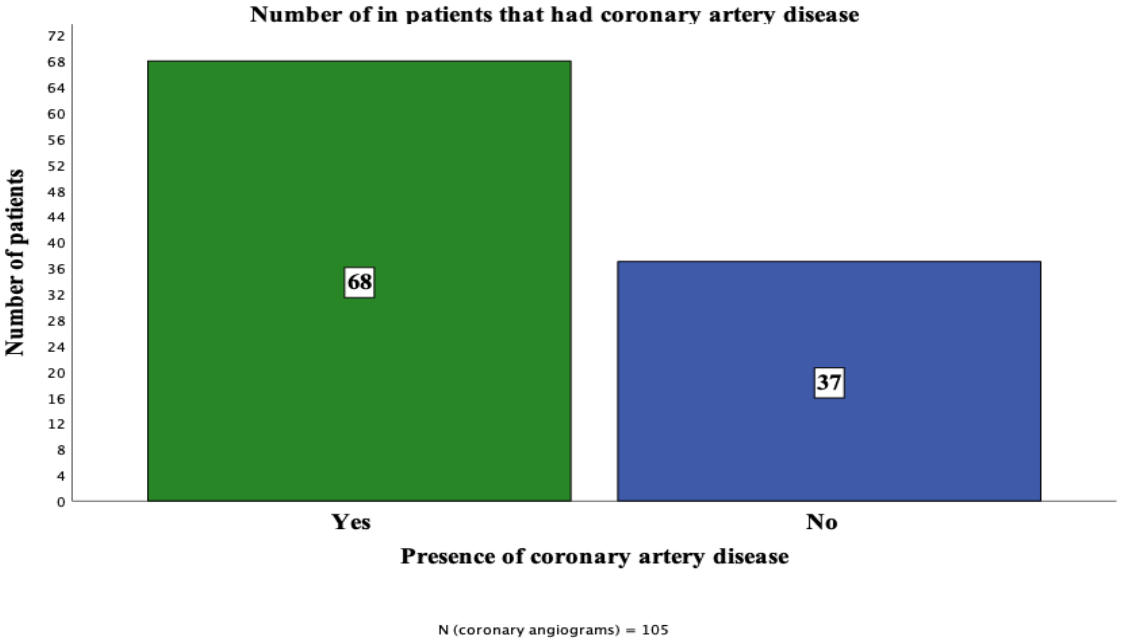


Figure 4.1.1: The prevalence of CAD from a coronary angiogram cohort

The 37 non-CAD individuals were composed of 25 males and 12 females. Males had ages ranging between 40 and 76 years, whilst females were between 36 and 75 years. The mean ages were 55 and 50 years for males and females, respectively.

From the 68 individuals with CAD, 55 were male and 13 were female. The ages of males ranged between 33 and 84 years, and females between 36 and 75 years. The mean ages were 60 and 61 years for males and females, respectively.

4.1.2. MORPHOMETRIC ANALYSIS OF CORONARY ANGIOGRAM COHORT

Measurements of the length and diameter were conducted on each coronary artery from the angiogram cohort. The cohort compromises of two sets of individuals; those with or without CAD. Individuals with CAD were the experimental group, those without CAD were the standard. The mean values of the length and diameter of both sets were compared to test if there is a correlation that relates to the condition of the individual.

4.1.2.1. RIGHT CORONARY ARTERY

i. Length and diameter values according to sex in the standard and experimental group

In males without CAD the right coronary artery (RCA) was 11.39 cm in length. In females without CAD the mean length was 12.61 cm. In males with CAD the RCA had a mean length of 10.42 cm, and in females, the RCA had a mean length of 11.40 cm [Table 7].

The mean diameter of the RCA in males without CAD was 0.30 cm. In females it was 0.26 cm. The mean diameter of the RCA in males with CAD was 0.24 cm, and in females, it was 0.27 [Table 8].

ii. The correlation of the morphology of the standard and experimental group

A bivariate correlation test was conducted to contrast the morphology of the standard and experimental groups. The RCA lengths of both groups had a Pearson correlation $r = 0.19$. This indicated a very weak correlation/no association between the RCA lengths of healthy patients and those that are diseased. The p-value > 0.05 showed that the data did not have statistical significance [Table 7].

The RCA diameters of healthy individuals had a very weak/no association, r = 0.197, with the RCA diameters of diseased individuals. The p-value < 0.05 indicates that the correlation was statistically significant [Table 8].

4.1.2.2. LEFT CORONARY ARTERY

i. Length and diameter values according to sex in the standard and experimental group

The left coronary artery (LCA) had the largest diameter and the shortest length in comparison to other coronary arteries. In males without CAD the LCA had a mean length of 1.86 cm, and in females it was 1.47 cm. Males with CAD had a LCA mean length of 1.42 cm, and females, a 1.39 cm LCA mean length [Table 7].

The diameter of the LCA in males without CAD had a mean value of 0.44 cm, and females, it was 0.45 cm. The mean diameter of the LCA in males with CAD was 0.31 cm, and in females, it was 0.57 cm [Table 8].

ii. The correlation of the morphology of the standard and experimental group

The LCA lengths of individuals with and without CAD had a *r* value of 0.16 This is indicative of a very weak correlation/no association. The p-value > 0.05 shows no statistical significance [Table 7]. The LCA diameters had a *r* value of 0.09 showing a very weak correlation between the two groups. There was no statistical significance for the data (p-value > 0.05) [Table 8].

4.1.2.3. LEFT CIRCUMFLEX ARTERY

i. The length and diameter values according to sex in the standard and experimental group

In males without CAD the LCX had a mean length of 8.64 cm. In females the LCX had a mean length of 9.27 cm. In males with CAD the LCX mean length was 8.99 cm, and in females, it was 8.96 cm [Table 7].

The LCX in males without CAD had mean diameter of 0.24 cm, and in females, it was 0.21 cm. The mean diameter for males with CAD was 0.22 cm, and in females, it was 0.25 cm [Table 8].

ii. The correlation of the morphology of the standard and experimental group

The LCX lengths of individuals with and without CAD had a r value of -0.02. This is indicative of a very weak negative correlation/no association. The P value > 0.05 shows no statistical significance. There is a very weak/no association (r = 0.02) between the LCX diameters of both groups, and the p-value > 0.05 which indicates no statistical significance.

4.1.2.4. ANTERIOR INTERVENTRICULAR ARTERY

i. The length and diameter values according to sex in the standard and experimental group

The anterior interventricular artery (AICA) is the longest coronary artery of the heart. In males without CAD the mean length was 12.06 cm; in females it was 12.83 cm. In males with CAD the AICA had a mean length of 12.04 cm, and in females, it was 12.45 cm [Table 7].

The diameter of the AICA in males without CAD had a mean diameter of 0.25 cm; in females, it was 0.20 cm. The mean diameter of the AICA in males with CAD was 0.52 cm, and in females, it was 0.31 cm [Table 8].

ii. The correlation between the morphology of healthy and diseased individuals

The AICA lengths of individuals with and without CAD had a *r* value of 0.23. This is indicative of a weak correlation/no association. The P value > 0.05 shows no statistical significance [Table 7]. There is a very weak/no association (r = -0.087) between the AICA diameters of both groups and the P value > 0.05 which indicates no statistical significance [Table 8].

4.1.2.5. POSTERIOR INTERVENTRICULAR ARTERY

i. The length and diameter values according to sex in the standard and experimental group

The posterior interventricular artery (PICA) in males with CAD was a length of 6.21 cm; in females the PICA had a mean length of 5.83 cm. The PICA in males with CAD had a mean length of 7.44 cm, and in females, it was 6.57 cm [Table 7].

The mean diameter in males without CAD was 0.15 cm, and in females, it was 0.34 cm. Males with CAD had a mean diameter of 0.19 cm, and in females, it was 0.18 cm [Table 8].

ii. The correlation between the morphology of healthy and diseased individuals

The PICA lengths of individuals with and without CAD had a r value of 0.23. This is indicative of a negative weak correlation/no association. The P value > 0.05 indicates no statistical significance [Table 7]. There is a very weak/no association (r = 0.067) between the PICA diameters of both groups and the P value > 0.05 which indicates that the null hypothesis is true [Table 8].

4.2. SUMMARY

The correlation tests conducted on individuals with and without CAD indicated a weak/no association. The weak association was observed for both length and diameter. This indicates that coronary artery length and diameter differs in individuals with CAD as compared to individuals without CAD. There was no statistical significance for most of the tests. There were twice as many coronary angiograms in the experimental group which could justify the p-values. Although, the RCA diameter, had a p-value < 0.05 which means the null hypothesis was rejected for that parameter.

Since, it has been established that the parameters of individuals with CAD differs from individuals without it, the mean±SD of individuals without CAD is considered the standard or norm.

Table 7: Summary of length values of the RCA, LCA, AICA, PICA and CX in standard (STD) and experimental (EXP) groups

		RCA STD	RCA EXP	LCA STD	LCA EXP	LCX STD	LCX EXP	AICA STD	AICA EXP	PICA STD	PICA EXP
Male	Mean ± SD (mm)	11.39 ±3.11	10.42 ±2.66	1.86 ±1.47	1.42 ±0.63	8.64 ±2.18	8.99 ±2.90	12.06 ±4.22	12.04 ±4.61	6.22 ±1.67	7.44 ±3.96
	Min-Max (mm)	5.62 - 19.11	5.07-17.47	0.81-9.41	0.62-3.63	4.01-14.04	5.00-20.37	1.11-24.40	6.45-38.79	3.45-9.78	3.13-16.75
Female	Mean ± SD (mm)	**12.61 ±2.78**	11.41 ±3.64	**1.47 ±0.29**	1.39 ±0.40	**9.27 ±2.94**	8.96 ±3.21	**12.82 ±3.34**	12.45 ±3.58	**5.83 ±1.37**	6.57 ±3.76
	Min-Max (mm)	8.71-16.01	6.41-20.09	0.96-1.86	0.54-2.61	5.71-14.02	4.71-15.50	8.38-17.47	9.18-21.76	3.70-8.74	3.29-16.75
Standard vs Experimental Groups	P-value	0.05		0.10		0.81		0.29		0.08	
	Pearson correlation (*r*)	0.19		0.16		-0.02		0.24		-0.17	

Table 8: Summary of diameter values of the RCA, LCA, AICA, PICA and CX in standard (STD) and experimental (EXP) groups

		RCA STD	RCA EXP	LCA STD	LCA EXP	LCX STD	LCX EXP	AICA STD	AICA EXP	PICA STD	PICA EXP
Male	Mean ± SD (mm)	0.30 ±0.08	0.24 ±0.09	0.43 ±0.16	0.31 ±0.12	0.24 ±0.06	0.22 ±0.09	0.25 ±0.08	0.52 ±1.86	0.15 ±0.10	0.19 ±0.17
	Min-Max (mm)	0.10-0.45	0.11-0.50	0.17-0.80	0.01-0.68	0.13-0.44	0.06-0.50	0.09-0.48	0.05-14.01	0.01-0.52	0.04-1.25
Female	Mean ± SD (mm)	**0.26 ±0.07**	0.28 ±0.07	**0.45 ±0.14**	0.57 ±1.10	**0.21 ±0.07**	0.25± 0.01	**0.20 ±0.07**	0.31 ±0.29	**0.34 ±0.41**	0.18 ±0.09
	Min-Max (mm)	0.12-0.37	0.16-0.36	0.13-0.67	0.11-4.21	0.11-0.38	0.13-0.43	0.11-0.35	0.12-0.68	0.06-1.33	0.07-0.35
Standard vs Experimental Groups	P-value	0.04		0.38		0.86		0.38		0.07	
	Pearson correlation (*r*)	0.19		0.09		0.18		-0.87		0.067	

4.3. BODY COHORT

4.3.1. DESCRIPTIVE STATISTICS

A total of 40 bodies were made available to UCT for 2021, only 37 were suitable for consideration. The age of the bodies had a range from 48 -105 years old, with a mean age of 76 years. The 3 bodies were excluded due to not being prepared for dissection or due to severe damage to the vessels due to prior teaching and learning.

The morphology of coronary arteries were deemed pivotal to the investigation since they determined the standard and experimental group for this study. From the 37 bodies a potential yield of 185 coronary arteries was expected. However, since 18 were missing (due to dissections), only 167 vessels were available for morphometric analysis [Table 9].

Table 9: The total number of coronary arteries missing from the body samples.

Coronary artery yield [a]

N	RCA yield	LCA yield	LCX yield	AICA yield	PICA yield
Available	34	35	33	31	34
Missing	3	2	4	6	3
Total	37	37	37	37	37

a. Sample type = Body

The yield of the vascular conduits was lesser than the coronary arteries obtained from the bodies. Out of a potential 185 vessels, 71 were missing, making the overall vascular conduit yield 114 [Table 10].

Table 10: The total number of vascular conduits missing from the body sample

Vascular conduit yield [a]

N	RITA yield	LITA yield	RA yield	RGEA yield	IEA yield	SV yield
Valid	25	34	28	20	19	25
Missing	12	3	9	17	18	12
Total	37	37	37	37	37	37

a. Sample type = Body

4.3.2. MORPHOMETRIC ANALYSIS

The mean±SD values of individuals without CAD from the coronary angiogram cohort was the standard norm used to contrast the morphometry of the coronary arteries from the body cohort.

Length and diameter values that deviated from the mean±SD of the norm, indicated bodies with coronary arteries with either some pathology or simply a variation that deviated from the standard.

The coronary arteries that deviated from the norm were measured to establish their mean length, diameter, and wall thickness. The samples that deviated from the norm were the ones compared with their corresponding vascular conduit. The rationale being that coronary arteries that were abnormal, are the ones most likely to be treated with CABG surgery.

The lengths and diameters of coronary arteries, obtained from bodies, were plotted on a scatter plot diagram according to age and sex. Red and black reference lines were added to indicate the mean of the standard, length [Table 7] and diameter [Table 8], of individuals with CAD. The standard deviation was indicated as values next to the reference lines.

4.3.2.1. RIGHT CORONARY ARTERY FROM THE BODY SAMPLE

Out of a sample of 37 bodies, 35 RCAs were obtained; 16 bodies were male and 19 were female. The mean length, diameter and wall thickness of the RCA in the body cohort was 11,44 cm, 0.34 cm, and 100.09 um, respectively. In relation to the RCA 7 male bodies deviated from the standard due to length (4) and/or diameter (4) [Figure 4.2.1b]. In the female samples only 8 RCA deviated from the standard group due to length [Figure 4.2.1a].

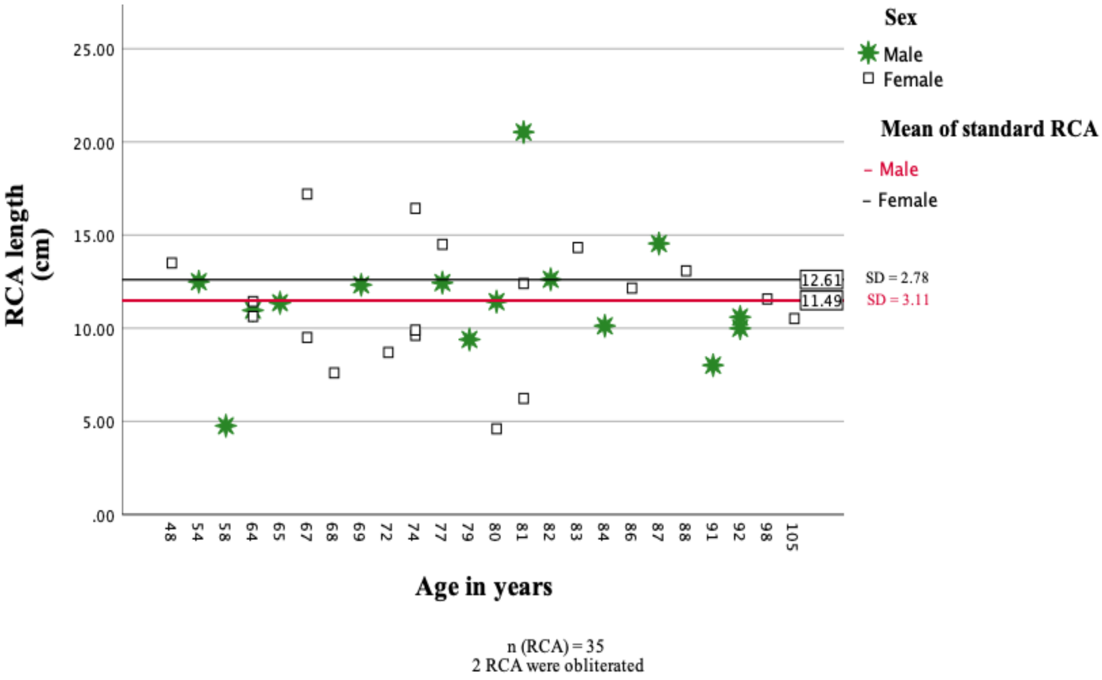
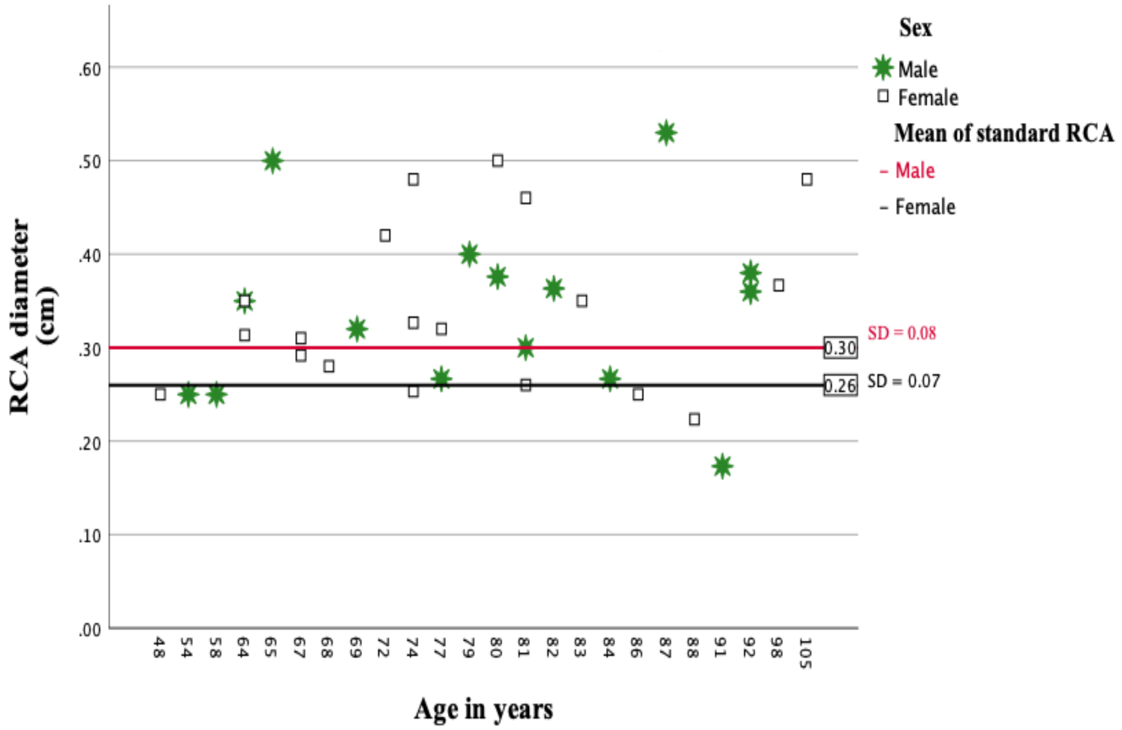


Figure 4.2.1a: The morphological deviation of cadaveric right coronary artery length from the mean standard of healthy individuals

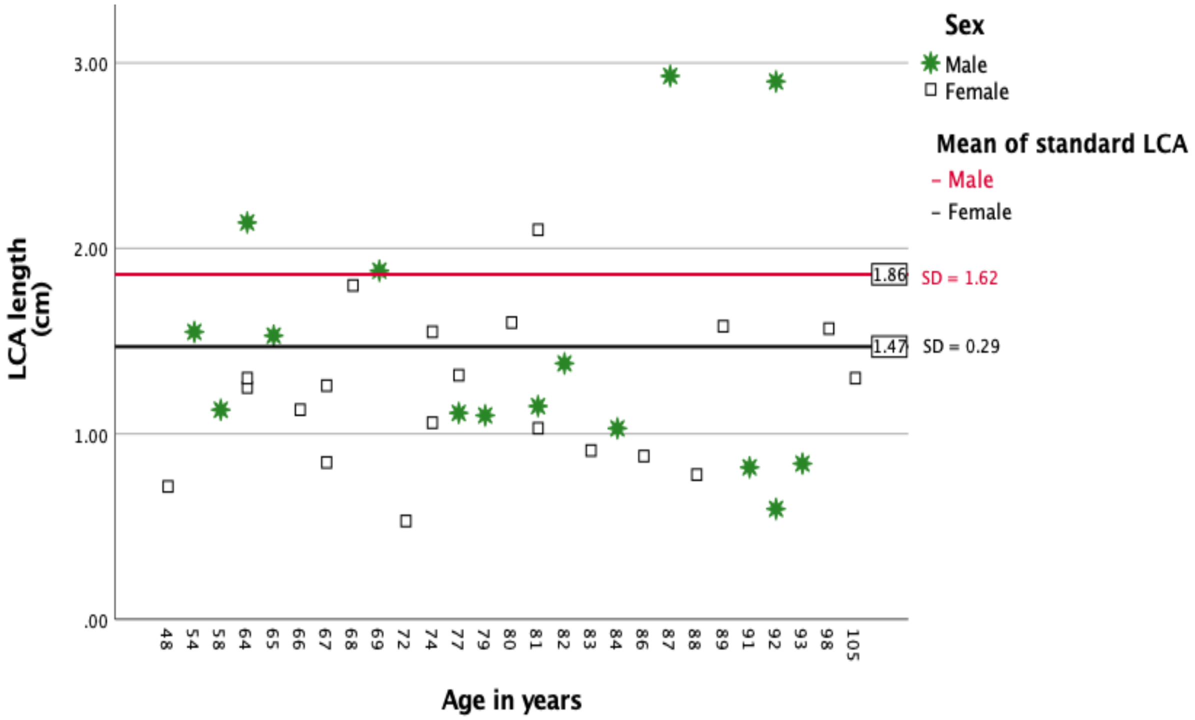


N (RCA) = 35
2 RCA were obliterated

Figure 4.2.1b: <u>The deviation of cadaveric right coronary artery diameter from the mean standard of healthy individuals</u>

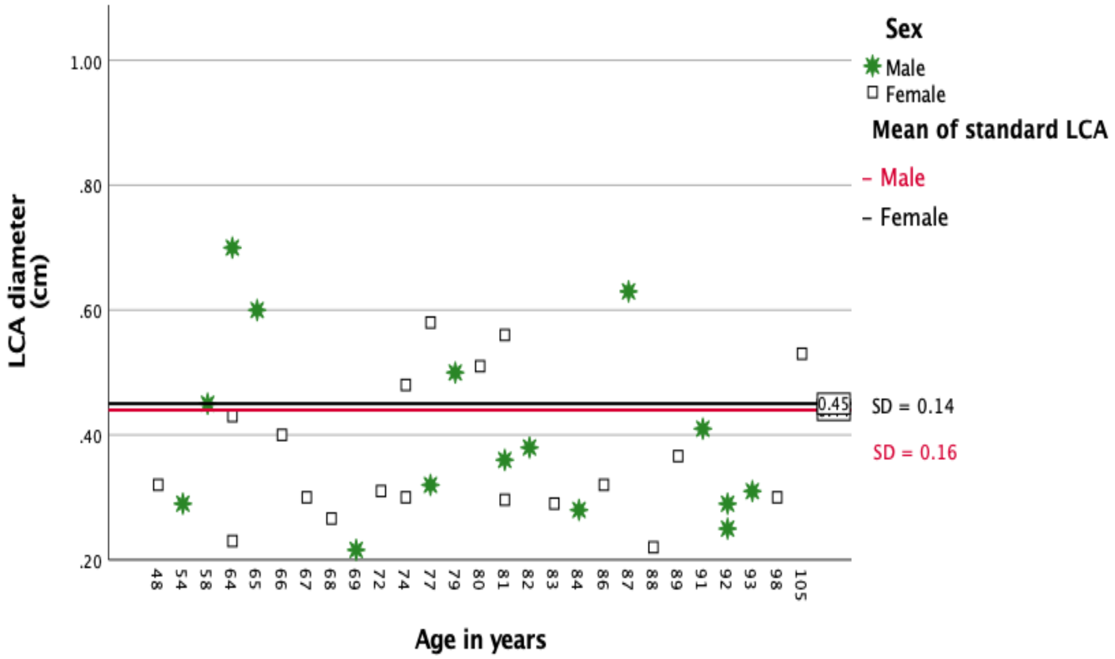
4.3.2.2. LEFT CORONARY ARTERY FROM THE BODY SAMPLE

From the bodies only 35 LCA samples were obtained; 15 bodies were male and 20 were female. The mean length, diameter and wall thickness for the LCA was 1.33 cm, 0.46 cm, and 129.73 um, respectively. In relation to the LCA, 4 male bodies deviated from the standard due to length, while 9 deviated due to diameter [Figure 4.2.2a]. In the female samples, 14 LCA deviated from the standard group due to length (5) or diameter (9) [Figure 4.2.2b].



N = 35
2 lCAs were oblitered

Figure 4.2.2a: <u>The morphological deviation of cadaveric left coronary artery length from the mean standard of healthy individuals</u>



N = 35
2 LCAs obliterated.
1 female aged 67 had a LCA diameter 1 > cm

Figure 4.2.2b: The morphological deviation of cadaveric left coronary artery diameter from the mean standard of healthy individuals

4.3.2.3. LEFT CIRCUMFLEX ARTERY FROM THE BODY SAMPLE

From the body cohort only 34 LCX were obtained; 14 bodies were male and 20 were female. The mean length, diameter, and wall thickness was 7.72 cm, 0.30 cm, 82.80 um, respectively. For the male bodies 10 LCX samples deviated from the standard due to length (6) or/and diameter (5) [Figure 4.2.3a]. In the female bodies, 9 LCX samples deviated from the standard group due to length (6) or/and diameter (6) [Figure 4.2.3b].

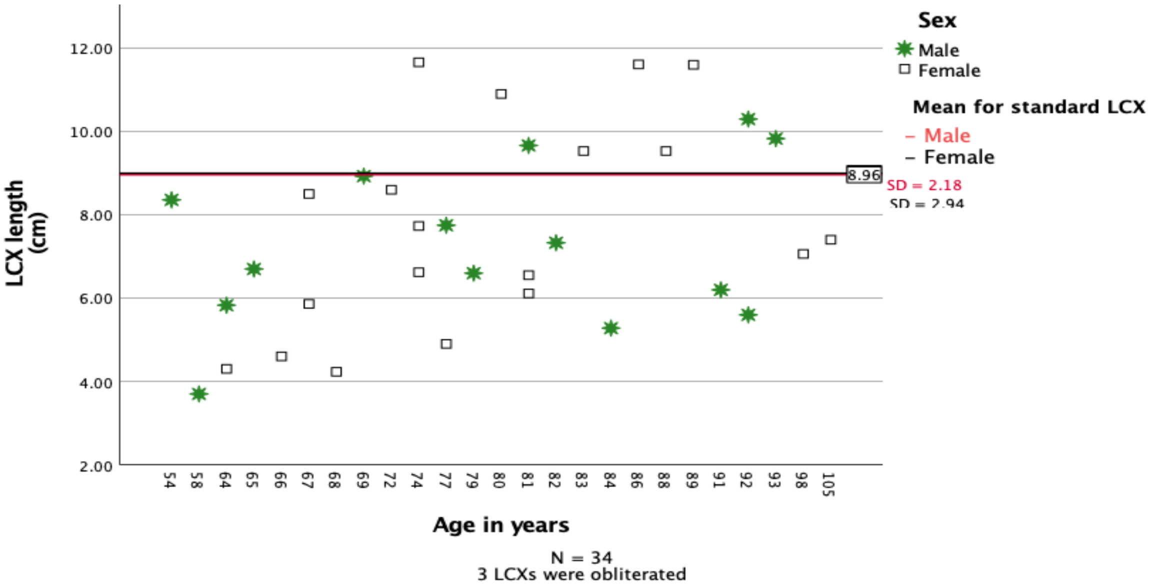
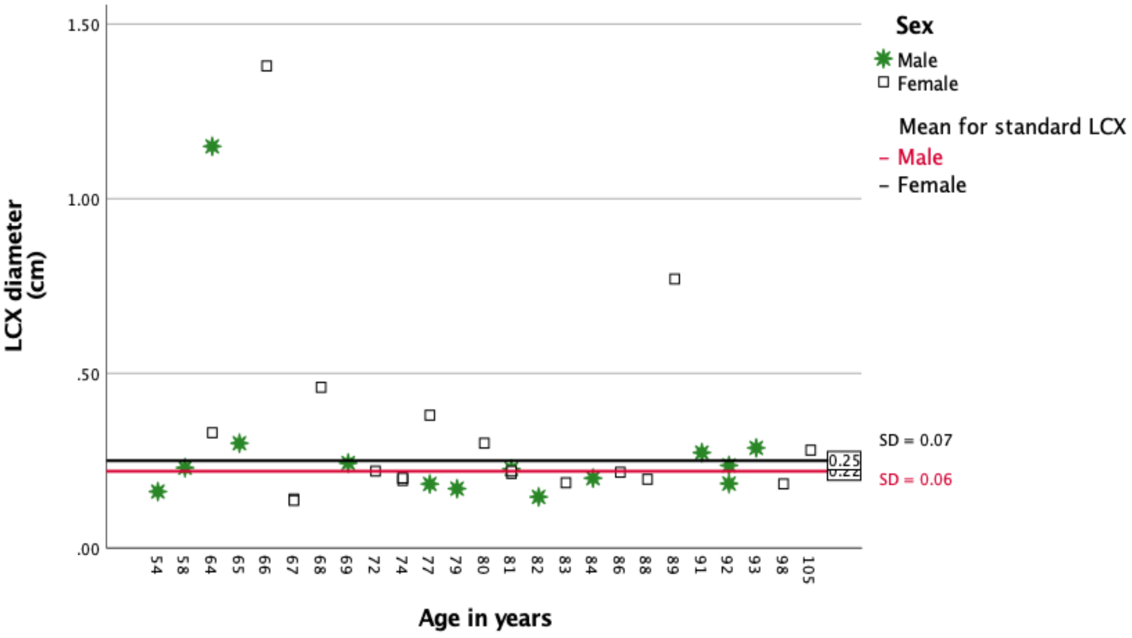


Figure 4.2.3a: The morphological deviation of cadaveric left circumflex artery length from the mean standard of healthy individuals

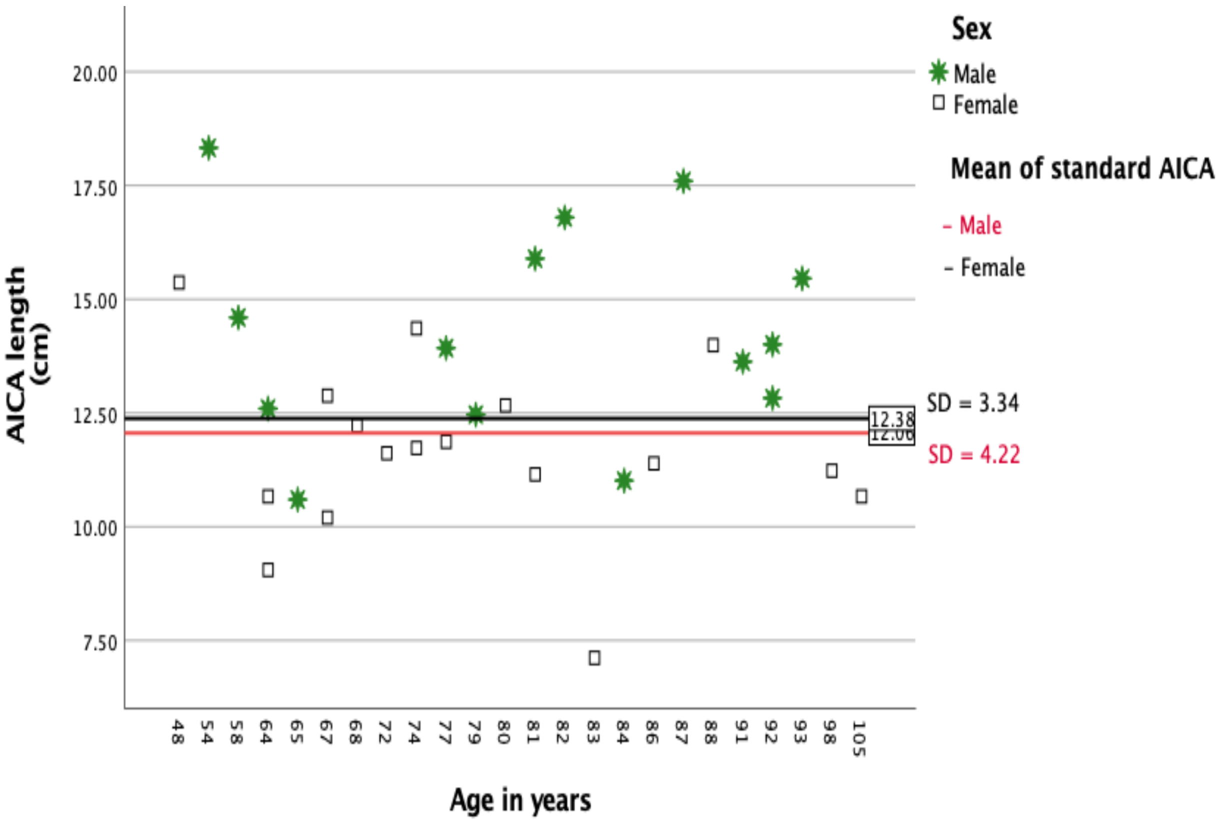


N = 34
3 LCXs were obliterated

Figure 4.2.3b: The morphological deviation of cadaveric left circumflex artery diameter from the mean standard of healthy individuals

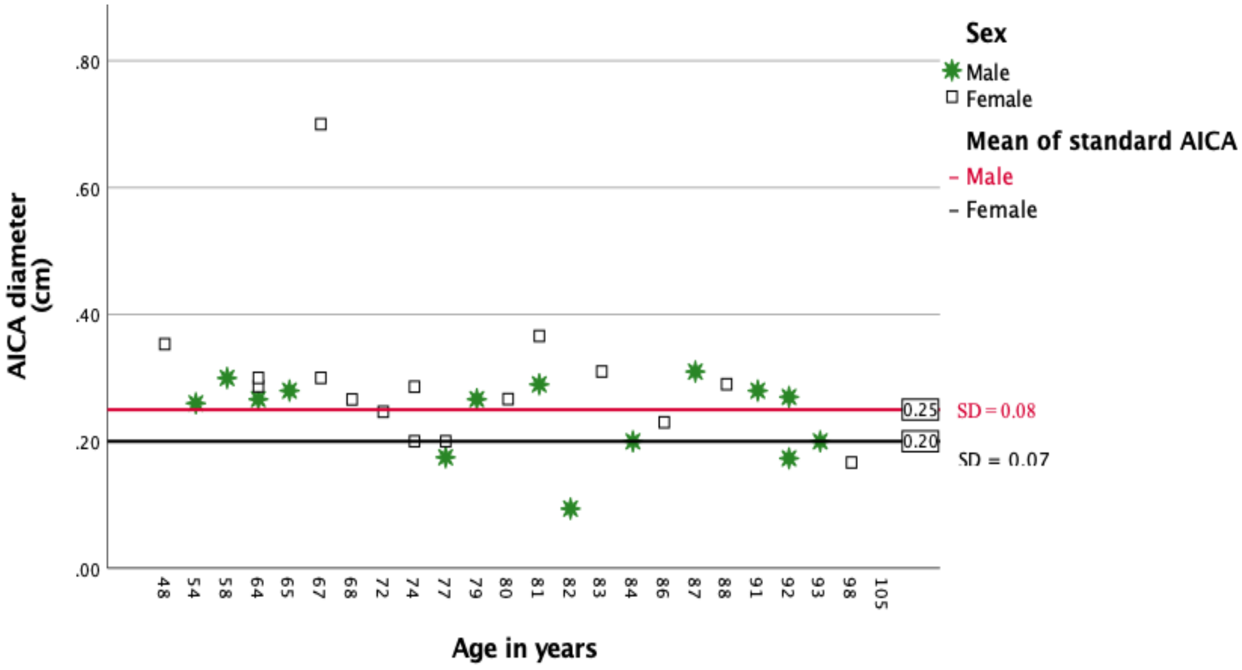
4.3.2.4. ANTERIOR INTERVENTRICULAR CORONARY ARTERY FROM BODY SAMPLE

The AICA yield from the body cohort was 31 samples; 14 bodies were male and 17 were female. The mean length, diameter, and wall thickness was 12.83 cm, 0.34 cm, and 82.80 um, respectively. In relation to the AICA 3 male bodies deviated from the standard due to length (3) and diameter (1) [Figure 4.2.4a]. In the female samples, 2 AICA deviated from the standard group due to length (2) [Figure 4.2.4b].



N=31
6 AICAs were obliterated

Figure 4.2.4a: <u>The morphological deviation of cadaveric anterior interventricular coronary artery length from the mean standard of healthy individuals</u>

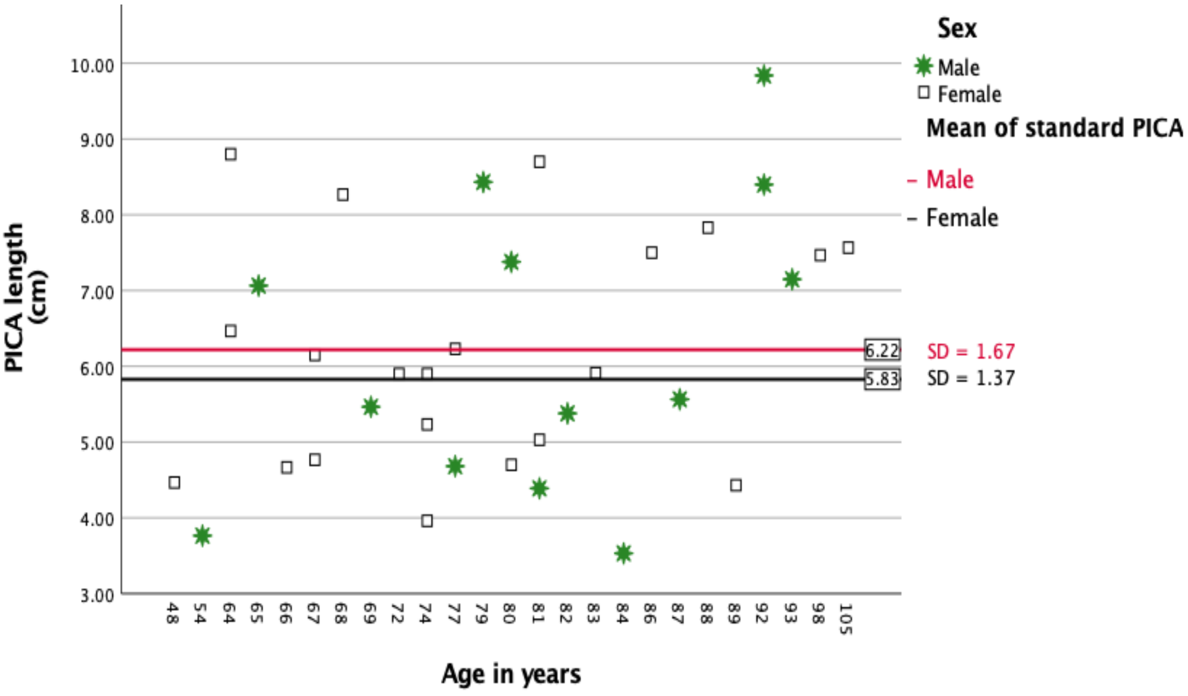


N = 31
6 AICAs were obliterated
Female aged 105 had an AICA diameter greater than 2cm

Figure 4.2.4b: The morphological deviation of cadaveric anterior interventricular coronary artery diameter from the mean standard of healthy individuals

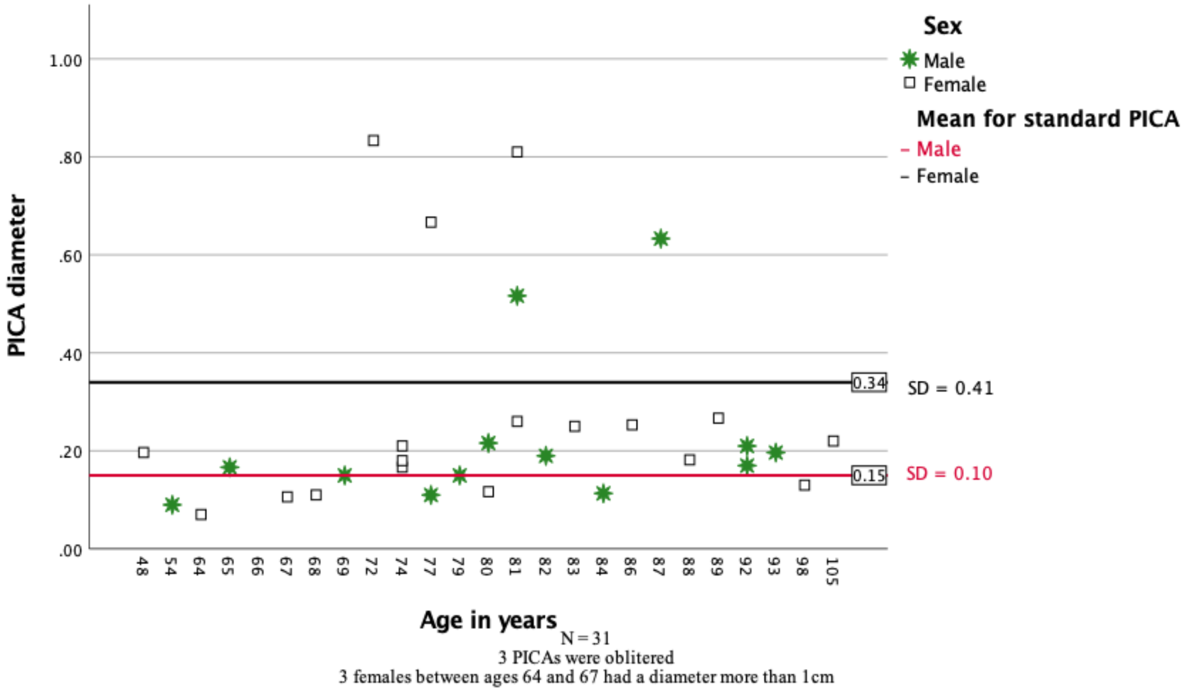
4.3.2.5. POSTERIOR INTERVENTRICULAR CORONARY ARTERY FROM THE BODY SAMPLE

From the body cohort 34 PICA samples were obtained; 13 bodies were male and 21 were female. The mean length, diameter, and wall thickness was 6.18 cm, 0.40 cm, and 82.80, respectively. In relation to the PICA samples 7 were from male bodies which deviated from the standard due to length (6) and/or diameter (2) [Figure 4.2.5a]. In the female samples, 13 PICA deviated from the standard group due to length (11) or diameter (5) [Figure 4.2.5b].



N = 34
3 PICAs were obliterated

Figure 4.2.5a: The morphological deviation of cadaveric posterior interventricular coronary artery length from the mean standard of healthy individuals



N = 31
3 PICAs were oblitered
3 females between ages 64 and 67 had a diameter more than 1cm

Figure 4.2.5b: <u>The morphological deviation of cadaveric posterior interventricular coronary artery diameter from the mean standard of healthy individuals</u>

All the coronary artery types, except the AICA, had 40% of the samples deviating from the standard group's mean±SD due to a smaller or bigger length and/or diameter. The coronary arteries that are outside the mean±SD of the standard group formed the experimental group for the bodies.

4.3.3. MORPHOMETRIC ANALYSIS OF THE CONDUITS

Measurements were conducted on the body cohort that deviated from the norm (Appendix 4). The mean values for the length, diameter, and wall thickness of the RITA were 15.81 cm, 0.21 cm, 87.9 um, respectively. The LITA had the following mean values for the length, diameter, and wall thickness; 16.21 cm, 0.31 cm, and 86.07 um.

The RA had a mean length, diameter, and wall thickness of 21.56 cm, 0.24 cm, and 100.83 um respectively. The mean length diameter and wall thickness for the SV was 34.5 cm, 0.30 cm, and 127.97 um.

The RGEA had a mean length, diameter and wall thickness of 14.04 cm, 0.18 cm, and 86.39 um respectively. The IEA had a mean length, diameter and wall thickness of 14.91 cm, 0.35 cm and 69.73 um.

4.3.4. A COMPARISON OF THE MORPHOLOGY OF CONDUITS AGAINST CORONARY ARTERIES

The net difference between coronary arteries and vascular conduits, from bodies that deviated from the norm, was calculated as an difference (Appendix 5). The difference is a net value that is found by subtracting the length or diameter of a conduit to a corresponding coronary artery. The y-axis is the length difference and the x-axis is for the diameter difference. When the x or y value > 0 then the vascular conduit is smaller and shorter in diameter and length relative to its corresponding coronary artery, respectively.

When the x or y value < 0 then the vascular conduit is larger and longer in diameter and length relative to the coronary artery, respectively. In instances where the x or y value = 0 then the vascular conduit is similar to the coronary artery. Each data point represents a single body [Figure 4.3.1].

4.3.4.1. THE DIFFERENCE BETWEEN RIGHT CORONARY ARTERY AND VASCULAR CONDUIT GRAFTS

The RITA and LITA share a similar distribution in the way they compare to the RCA. The SV in most cases had a longer length comparison to the RCA. Apart for a few outliers (RITA, LITA, and IEA) the diameter for most conduits was relatively similar to the RCA diameter ranging between -0.50 and 0.50 [Figure 4.3.1].

The RITA, LITA and IEA had length and diameter indices that are quite similar in range. The RA had a mean diameter difference that is the largest. The SV had a length mean difference that is the largest [Table 11].

Figure 4.3.1: Length and diameter difference right coronary artery and other vascular conduits

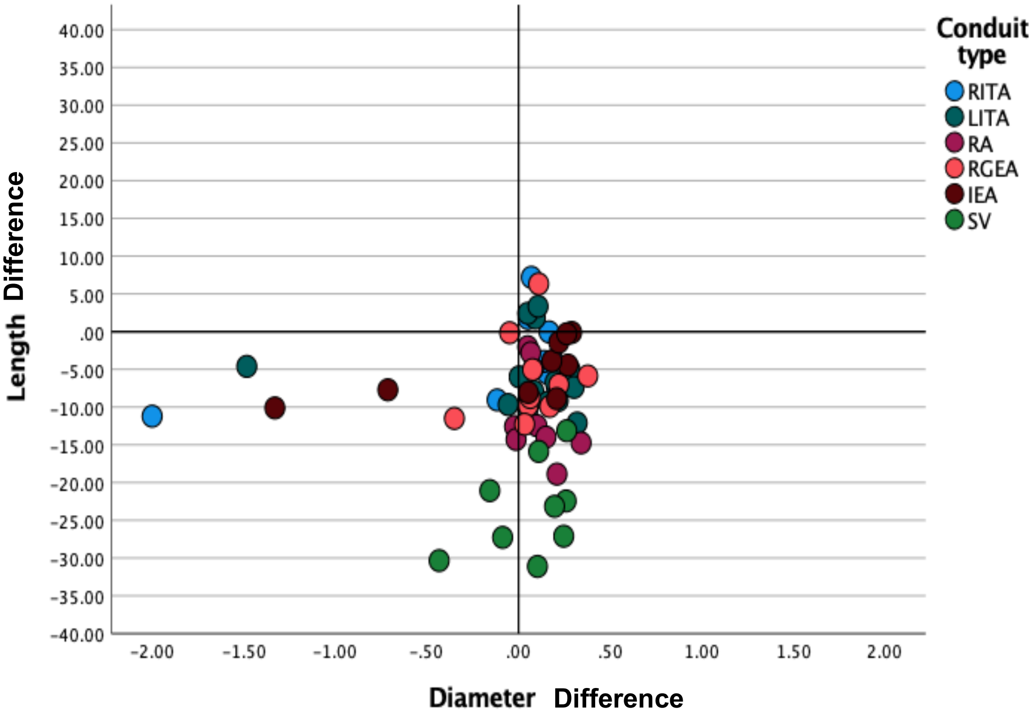


Table 11: Length and diameter difference between the right coronary artery and six vascular conduits

Conduit	Length difference range	Length mean difference	Diameter difference range	Diameter mean difference
RITA	-11.2 to 7.4	-3.55	-2.0 to 0.21	-0.12
LITA	-12.1 to 3.35	-5.76	-1.48 to 0.32	0.02
RA	-18.87 to -2.0	-10.73	-0.21 to 0.34	0.11
RGEA	-12.26 to 6.33	-6.39	-0.35 to 0.38	0.07
IEA	-10.10 to -0.10	-4.98	-1.33 to 0.29	-0.06
SV	-27.25 to -13.12	-23.49	-0.43 to 0.26	0.06

4.3.4.2. THE DIFFERENCE BETWEEN LEFT CORONARY ARTERY AND VASCULAR CONDUIT GRAFTS

Most of the conduits had a diameter difference that is positive and all that had the lengths were negative; this indicates that the LCA is short compared to all conduits and it tends to have a larger diameter. The SV, RA and RGEA had at least two cases where their diameter was similar to the LCA's diameter [Figure 4.3.2].

The SV and RA length mean difference indicates that they had a relatively longer length compared to the LCA. The RITA, LITA and IEA had the three shortest mean length indices [Table 12]. All of the diameter mean length indices were positive; this indicates that the LCA has a diameter that is generally larger. The most similar conduit was the RA in relation to diameter.

Figure 4.3.2: Length and diameter difference of the left coronary artery and other vascular conduits

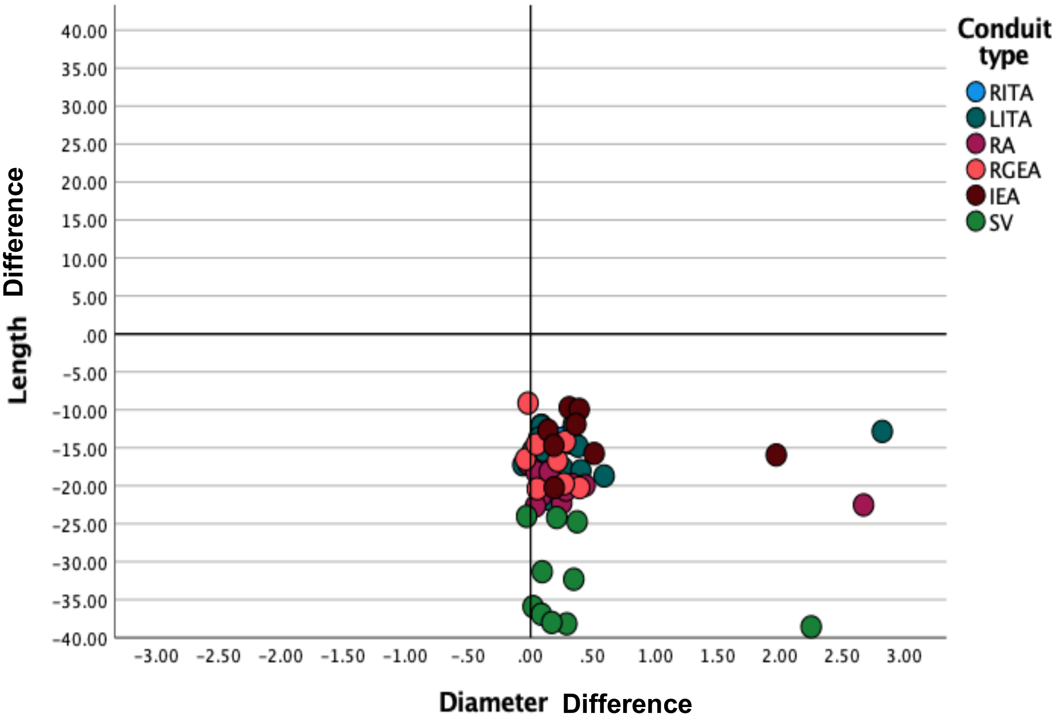


Table 12: Length and diameter difference between the left coronary artery and six vascular conduits

Conduit	Length difference range	Length mean difference	Diameter difference range	Diameter mean difference
RITA	-18.78 to -10.7	-14.47	0.06 to 0.36	0.17
LITA	-21.76 to -11.92	-15.35	-0.06 to 2.82	0.38
RA	-22.65 to -17.07	-20.15	-0.02 to 2.67	0.04
RGEA	-20.38 to -9.10	-16.42	-0.04 to 0.39	0.15
IEA	-20.23 to -9.70	-13.85	0.14 to 1.97	0.51
SV	-38.56 to -24.02	-32.41	-0.03 to 2.25	0.38

4.3.4.3. THE DIFFERENCE BETWEEN LEFT CIRCUMFLEX ARTERY AND VASCULAR CONDUIT GRAFTS

The RITA and LITA length and diameter difference are distributed in a similar pattern, when compared to the LCX. Most of the conduits had a diameter that is distributed close to the origin, indicating similarity with their corresponding coronary artery. All the conduits, except the SV, had outliers [Figure 4.3.3]. The RITA, LITA, and SV have a mean diameter that indicates that they are very similar to the LCX [Table 13].

Figure 4.3.3: Length and diameter difference of the left circumflex artery and other vascular conduits

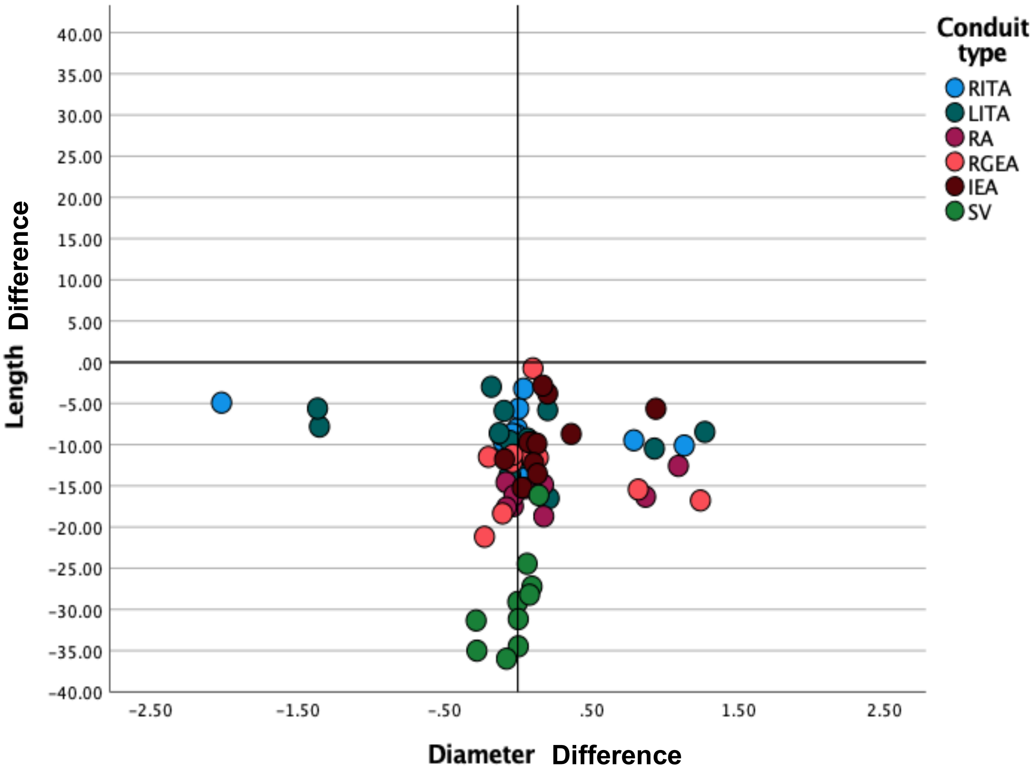


Table 13: Length and diameter difference between the left circumflex artery and six vascular conduits

Conduit	Length difference range	Length mean difference	Diameter difference range	Diameter mean difference
RITA	-13.40 to -3.2	-8.45	-2.02 to 1.13	-0.03
LITA	-16.50 to -2.97	-9.41	-1.36 to 0.93	-0.04
RA	-18.69 to -9.67	-15.32	-0.08 to 1.09	0.22
RGEA	-18.33 to -0.73	-13	-0.23 to 1.24	0.17
IEA	-15.21 to -2.83	-9.33	-0.09 to 0.94	0.21
SV	-35.97 to -16.13	-29.30	-0.28 to 0.14	-0.03

4.3.4.4. The difference between anterior interventricular artery and vascular conduit grafts

The conduit diameter indices were distributed around origin with the SV being the most similar to the AICA. The LITA and RITA length and diameter patterns were closely distributed to each other. The RGEA and IEA also shared a similar distribution [Figure 4.3.4].

The RITA, LITA, and IEA length indices were similar. The RGEA and SV had diameter mean differences that are the same [Table 14].

Figure 4.3.4: Length and diameter similarity of the anterior interventricular coronary artery and other vascular conduits

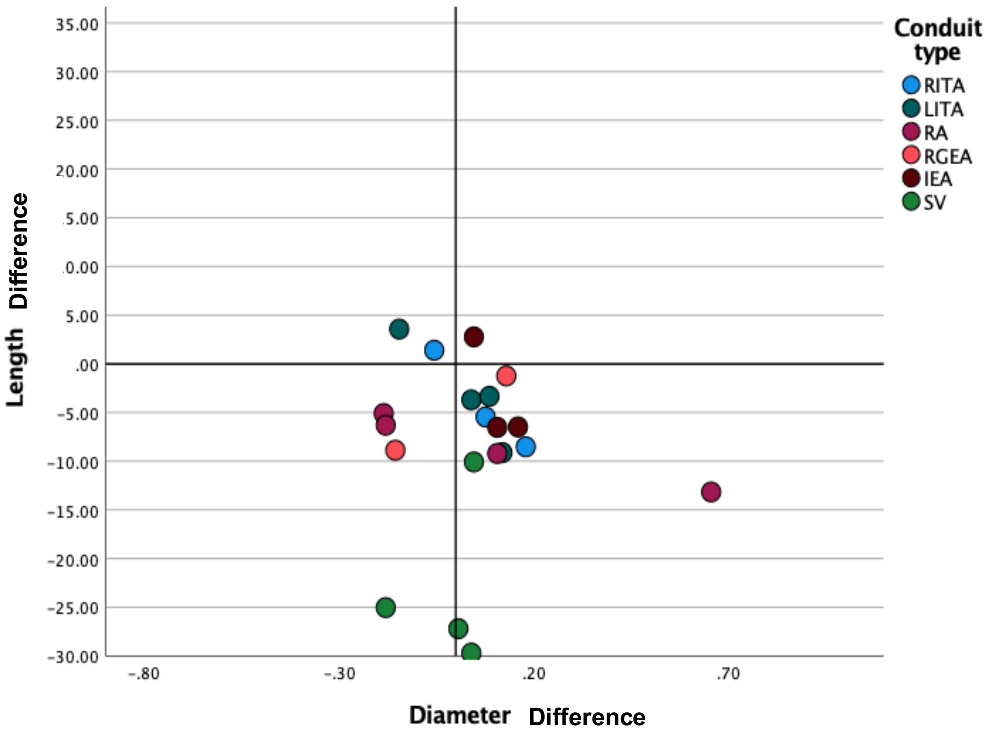


Table 14: Length and diameter difference between the anterior interventricular coronary artery and six vascular conduits

Conduit	Length difference range	Length mean difference	Diameter difference range	Diameter mean difference
RITA	-8.51 to 1.40	-4.19	-0.06 to 0.18	0.07
LITA	-9.11 to 3.57	-3.14	-0.15 to 0.12	0.03
RA	-13.15 to -5.10	-8.44	-0.19 to 0.66	0.1
RGEA	-8.87 to -1.24	-5.01	-0.16 to 0.13	-0.02
IEA	-6.52 to 2.77	-3.4	0.16 to 0.05	0.12
SV	-29.69 to -10.07	-23.0	-0.18 to 0.05	-0.02

4.3.4.5. THE DIFFERENCE BETWEEN POSTERIOR INTERVENTRICULAR ARTERY AND VASCULAR CONDUIT GRAFTS

Most of the conduits had a diameter that is slightly bigger than the PICA. The SV and RITA had a high number of conduits that matched the PICA. All the conduits were longer than the PICA [Figure 4.3.5].

The RITA, LITA, RGEA and IEA had a length mean difference that closely related to one another. The RA and SV had a greater difference, indicating that both conduits were much larger than the PICA. The RGEA and LITA had a diameter mean difference that is very close to zero, indicating that the diameter for both conduits were similar to the PICA [Table 15].

Figure 4.3.5: Length and diameter difference of the posterior interventricular coronary artery and other vascular conduits

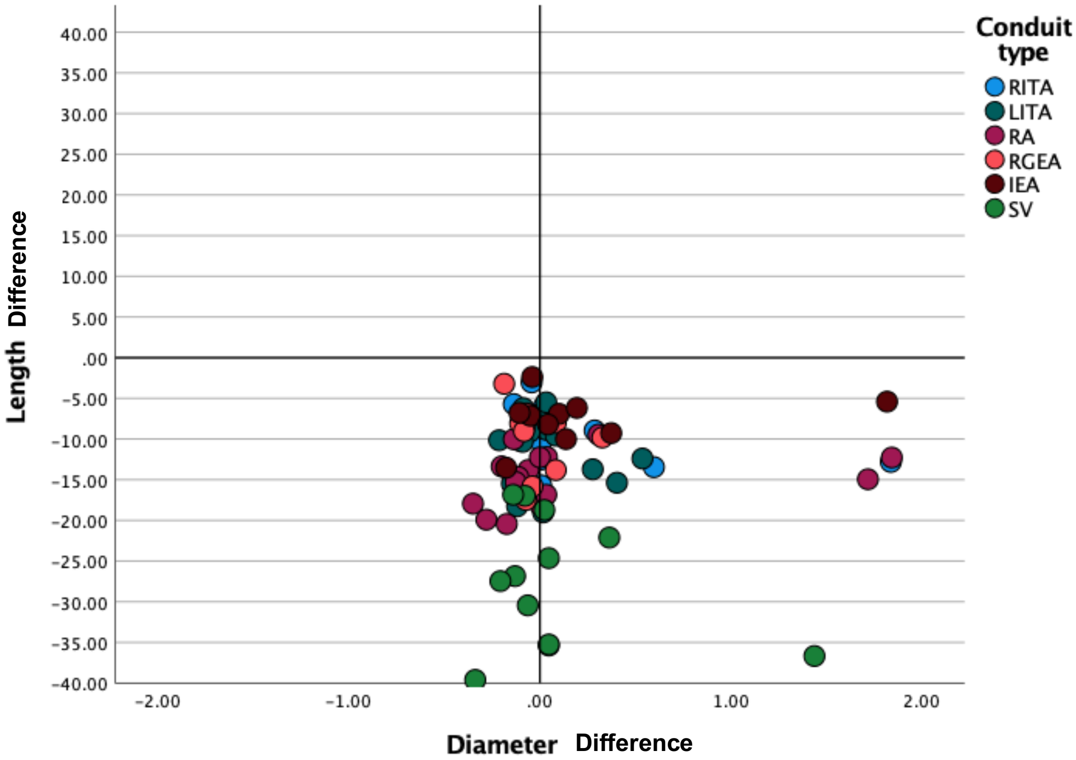


Table 15: Length and diameter difference between the posterior interventricular coronary artery and six vascular conduits

Conduit	Length difference range	Length mean difference	Diameter difference range	Diameter mean difference
RITA	-15.68 to -3.03	-8.98	-0.14 to 1.84	0.18
LITA	-19.01 to -5.48	-10.95	-0.21 to 0.54	0.03
RA	-20.44 to -9.45	-14.76	-0.35 to 1.84	0.17
RGEA	-17.48 to -3.20	-10.07	-0.19 to 0.33	0.01
IEA	-13.52 to -2.37	-7.57	-0.18 to 1.82	0.23
SV	-39.59 to 16.84	-27.57	-0.34 to 1.44	0.08

4.4. SURVEY OF CARDIOTHORACIC SURGEONS IN SOUTH AFRICA

A survey was disseminated amongst members of the South African Society of Cardiothoracic Surgeons (SCTSSA). From the entire SCTSSA membership 9 individuals interacted with the survey but 4 responses were not considered in accordance with the exclusion criteria. The survey had four main categories; informed consent, demographic data, conduits frequently used by clinicians, decision-making under certain clinical scenarios, and factors that may affect conduit selection.

4.4.1. CLINICAL EXPERIENCE AND PREFERRED USE OF VASCULAR CONDUITS

All the respondents were qualified cardiothoracic surgeons with the role of consultants. They all worked in different hospitals, 60% (n=3) worked in private practice, while the remaining 40% worked in public academic hospitals. All surgeons conduct at least 10 CABG procedures annually; 60% have been conducting CABG surgery for less than 10 years. The remaining (n=2) 40% having been conducting the procedure for more than 10 years [Figure 4.4.1].

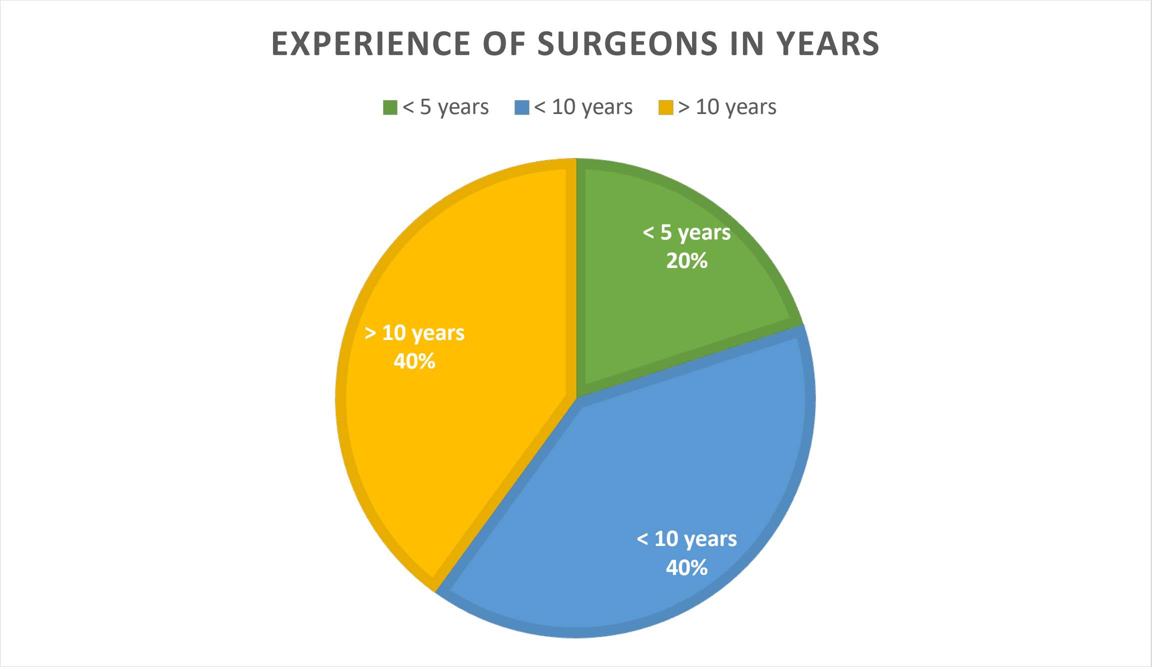


Figure 4.4.1: Distribution of surgeon experience according to years performing CABG surgery.

All the clinicians preferred to use at least three of following conduits; RITA, LITA, RA, and SV [Figure 4.4.2]. Only two clinicians indicated their preferred use of the RITA and LITA. In most instances the RITA or LITA was paired with the RA and SV [Figure 4.4.2].

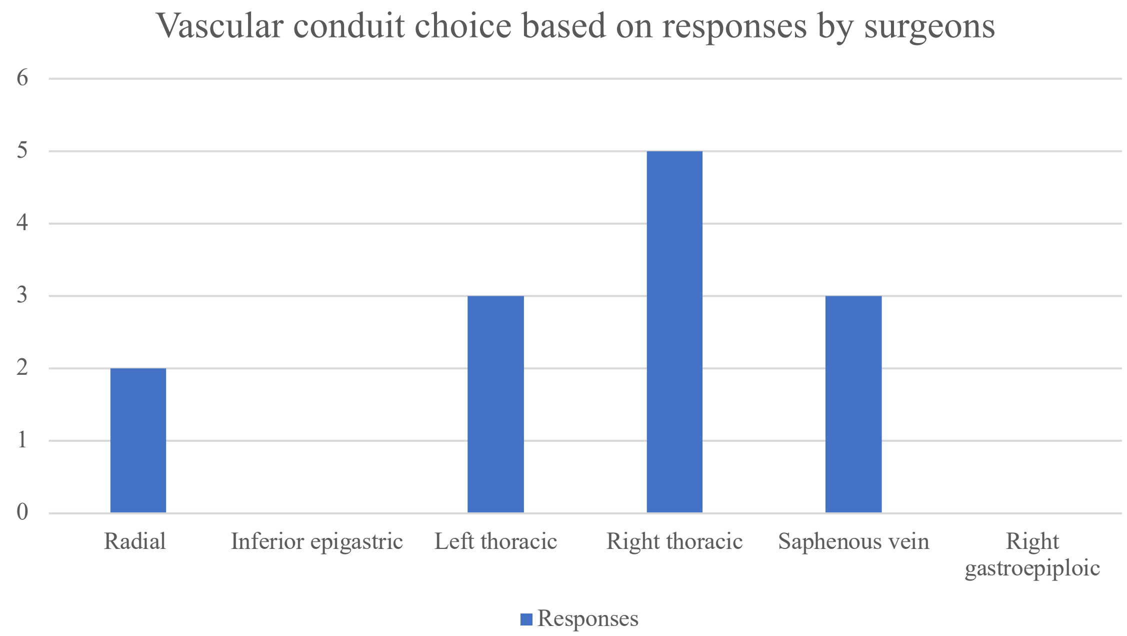


Figure 4.4.2: Vascular conduit grafts commonly used by a cohort of South African surgeons

4.4.2. CONSIDERATIONS UNDER DIFFERENT CLINICAL SCENARIOS

Surgeons were given a series of clinical scenarios. The first scenario asked the importance of using bilateral thoracic arteries for grafting in a typical low risk patient in whom there is a plan for 3 – 4 distal anastomoses, who also has good left ventricular function. From the cohort 40% (n=5) of surgeons indicated that it is very important, while the remaining 60% indicated that it is least important. These responses corresponded with the initial answers given about conduit preference. Surgeons were also asked if they would skeletonize (resect the vessel from all surround tissue) the thoracic arteries in the same scenario. Only the two who thought the bilateral use of the ITA was very important agreed; the rest disagreed.

In the same scenario clinicians were asked the importance of using the appropriate anastomosis. They were asked how important it is for the graft to serve only one distal anastomosis rather than sequential, T or Y configurations [Figure 2.5]. Only one surgeon disagreed that it is not important; the remaining surgeons agreed that one distal anastomosis is very important. The last question given in this scenario asked surgeons to describe their decision-making if the patient was frail and had comorbidities. Three surgeons recommended the use of the SV graft with some indicating that it reduces bypass time, while two said their treatment would not change. The two surgeons whose approach would not change are the same individuals who disagreed with the bilateral use of the thoracic arteries.

Clinicians were asked about the importance of using arterial grafts in a typical patient with good left ventricular function. Two indicated that it is very important, whilst another two disagreed with its importance. Only one clinician indicated their average consideration for its importance.

The final scenario related to percutaneous coronary intervention (PCI). A patient undergoing PCI in the Cath lab was brought for emergency surgery. Surgeons were asked whether their practices would change. All surgeons indicated that given it would be an unexpected emergency situation – they would use a venous graft. Only one surgeon suggested using the LITA solely.

4.4.3. OTHER FACTORS THAT MAY AFFECT CONDUIT SELECTION

This section of the survey aimed at ascertaining other factors that influence a surgeon's decision when it comes to conduit selection. Surgeons with 5 or more years of experience tended to rely more on their experience, whilst the one with less than five relied more on high quality literature, as opposed to their experience conducting CABG.

The surgeon with more than two decades of experience also indicated the importance of using the opportunity as a training experience for junior registrars. All surgeons did consider literature and with equal consideration the competence of the team assisting with the graft harvesting.

CHAPTER 5: DISCUSSION

The results of this study indicate that the diameter of coronary arteries varied between individuals who had CAD and those without, thus confirming the hypothesis. The null hypothesis that Although, the null hypothesis was only rejected for the RCA, all the coronary arteries between the two groups showed a weak Pearson correlation. The different morphology between healthy and diseased individuals will be discussed.

The coronary arteries belonging to different sexes indicated a small or, in some instances, negligible difference. This indicates that while sex-related variations exist, stronger deviations may occur for parameters like diameter and wall thickness due to pathologies or age. From the entire body sample, a majority of the hearts had at least one coronary artery that was considered to deviate from the standard group. Those arteries were measured and the mean values of the wall thicknesses were contrasted against the conduits for the same parameter.

A similar comparison was done for the bodies in the experimental group using indices that show the net length or diameter value between the coronary arteries and conduits. The mean measurements were also ascertained for these indices to not only indicate the relationship between the graft and conduit but also amongst the conduits themselves to rank their suitability. Factors such a surgeon's choice will be discussed in light of the quantitative data, to assist with creating the contexts in which certain grafts are more suitable than others.

This chapter will start by discussing the results of the gross anatomy of coronary arteries as it relates to age and sex. This will be followed by the description of the standard group – and the results emanating from comparing coronary arteries amongst themselves. Finally, the results of the arterial wall thicknesses, length, and diameter comparisons will be discussed and used to consider the suitability of particular vascular conduits over others.

5.1. SAMPLE DEMOGRAPHICS

5.1.1. PATIENTS IN THE CORONARY ANGIOGRAM REPOSITORY

From the entire coronary angiogram repository 76% were men between the ages 33 and 84. Although, there were twice as many people with CAD compared to those without, men still made up 80% of the positive cases. This confirms the assertion that South African men who are approaching their 40s are more likely to be diagnosed with CAD (Burger et al., 2016). The mean age of individuals, from the coronary angiogram cohort, with CAD and those without ranged from 50 to 61 years old for both sexes. The mean age for patients scanned for CAD is just below the age (65 years) that epidemiological studies in the SSA have noted as the age when ischaemic heart disease is mostly like to occur (Onen, 2013, Yao et al., 2022).

Individuals that did not have CAD were considered the standard. There were 37% healthy individuals in the entire repository. Since the sampling method was purposive instead of randomized, any inferences about the general population might not be warranted. However, the lack of healthy patients in the repository indicates that older patients who experience symptoms associated with CAD are most likely going to be diagnosed with the pathology (Yuyun et al., 2020). This may be due to increased occlusions which result in increased heart rates, chest pains, or heart palpitations (Aribas et al., 2022). The slow-progressive nature of atherosclerosis is well described in literature, meaning patients who are usually screened for CAD are most likely to have moderate to acute occlusions (Gray et al., 2019).

There is no association between the coronary artery length and diameter of individuals with and without CAD. In 3 out 5 coronary arteries from the standard group a larger mean diameter was observed. Prolonged atherosclerosis is known to induce cellular remodelling and hyperplasic changes which can reduce the diameter of the lumen due to increased plaque (Yang et al., 2018, Gustafson, 2010). The AICA and PICA standards were the only coronary arteries without a larger mean diameter compared to its diseased counterparts. This could be attributed to the fact that atherosclerosis affects different coronary arteries in a different way (Mtz et al., 2015). The RCA, LCA and the LCX are known to be susceptible to atherosclerotic changes due to their bifurcations creating hemodynamic disturbances (Chatzizisis et al., 2007, Mtz et al., 2015).

However, narrowing of the blood vessel is not the only possible outcome of cellular remodelling. In many other instances it is possible for the diameter to increase as a result of vasodilation (Maruhashi et al., 2018). This is a common phenomenon in aneurysmal formation (Jiang et al., 2017). The RCA is the only coronary artery where the null hypothesis was rejected, indicating with a degree of certainty that the standard group's mean diameter differs from its diseased counterpart.

5.1.2. STANDARD CORONARY ARTERY LENGTH AND DIAMETER

The mean RCA length and diameter of patients in the standard group was 11.39 cm and 0.30 cm respectively, in males. For females the RCA length and diameter was 12.61 cm and 0.26 cm, respectively. The data obtained from the RCA diameter between the sexes was significant with a p-value = 0.04. The length was greater in females as opposed to males. A study in Mexico and Turkey found the mean values for length to be 12.69 ± 1.94 cm and 6.60 ± 1.53 cm in RCA (ÜnlÜ et al., 2003, Hernández et al., 2013). The mean RCA length for South African males and females seemed to be closer to the Mexican study in comparison to the one conducted in Turkey. There could be many reasons for this. One of the factors may be the physiological differences, informed by environmental factors, that exist in the CVS of people in the Northern versus Southern Hemisphere (Marti-Soler et al., 2014). There are environmental determinants that affect the cardiovascular system i.e. prolonged winters increasing glucose and blood pressure levels (Bhatnagar, 2017).

The mean LCA length and diameter for males was 1.86 cm and 0.43 cm, respectively; and for females the length was 1.47 cm and 0.45 cm for diameter. A study conducted in South Africa showed that the LCA lengths varied between a mean length range of 1.01 cm to 1.48 cm, and the diameter ranged from 0.38 cm to 0.5 cm depending on the branching pattern and angle of division (Ajayi et al., 2013). The LCA in the standard group did not deviate from other South African studies.

The LCX had a mean length and diameter of 8.64 cm and 0.24 cm respectively for males. In females the mean length was 9.27 cm and the diameter was 0.21 cm. In a Mexican study the length was 8.89 ± 2.11 cm for CX (Hernández et al., 2013). In a Turkish study the LCX length was 5.70 ± 1.20 cm (ÜnlÜ et al., 2003). Less than half the bodies (< 48%), had a LCX length or diameter that was within the mean ± SD. The LCX is one of the few coronary arteries known to be more susceptible to occlusions (Rösch and Rahimtoola, 1977).

The AICA had a mean length and diameter of 12.06 cm and 0.25 cm respectively in males. In females the mean length and diameter was 12.84. cm and 0.20 cm, respectively. A study in Turkey showed the mean to be 9.38 ± 1.84 cm (ÜnlÜ et al., 2003), in a Mexican study the mean length was 15.66 ± 1.12 cm (Hernández et al., 2013). Less than 15% of the bodies had at least one AICA that deviated from the standard. The PICA had a mean length and diameter of 6.22 cm and 0.15 cm, respectively, in males. For females the mean length and diameter is 5.83 cm and 0.34 cm, respectively.

The mean lengths and diameters of male and female coronary arteries in the standard group were within the general range of studies done either in the country or other places in the world. The PICA did not have many studies done on it, apart from studies that look at dominance. At least 73% of the PICA emerged from the RCA, meaning, cadavers were mostly right dominant.

5.1.3. CORONARY ARTERIES FROM THE BODIES IN CONTRAST TO THE STANDARD

The body samples consisted mostly of females. South African studies have made the observation that body donor programs tend to have more females as opposed to males in modern times (Kramer et al., 2019, Kramer and Hutchinson, 2015). The entire body sample had an age range of 48 to 105.

More than 80% of the bodies used in this study had at least one or more coronary artery deviating from the standard group in relation to length and diameter. The lengths of the coronary arteries from the bodies had a more diversified range in relation to the mean ± SD of the standard group. The diameter trends were either visibly larger than the standard group, in other instances lower, and occasionally fairly distributed about the mean.

Most RCAs from the bodies were larger than the standard group samples. This could be as a result of prolonged endothelial dysfunction which contributes to vasodilation, in some instances lesion formations (Maruhashi et al., 2018). LCAs from the bodies mostly had smaller diameters in comparison to the standard group. The left main stem is one of the most frequently occluded coronary arteries, and when occlusion is total, it is potentially fatal due to the difficulty that it poses for resuscitation (Édes et al., 2018, Rösch and Rahimtoola, 1977).

The LCX is another vessel that tends to be occluded frequently (Mtz et al., 2015). The LCX from the bodies had a higher incidence of narrowed diameters, although the general trend was fairly distributed about the mean ± SD of standard group. This could be a combination of some LCX samples having a plaque induced decrease in the diameter or endothelial dysfunction which can reduce TM size (Yang et al., 2018). The mean age of the body cohort was above 74 years old which could further increase the risks for LCX narrowing. The PICA samples had a higher incidence of diameter or length deviations.

All the coronary artery samples that deviated from the standard were compared to all the conduits in that individual's body. The net difference between the two was used as an indicator to demonstrate whether a conduit is shorter, longer, or equal to the coronary artery.

5.2. SIMILARITY OF VASCULAR CONDUITS TO CORONARY ARTERIES OBTAINED FROM THE BODIES

5.2.1. THE LEFT AND RIGHT INTERNAL THORACIC ARTERY

The LITA and RITA had similar indices for coronary artery length comparisons. This confirms what has been reported in literature about the ITA being relatively equal in length bilaterally, or the difference between the two being negligible (Kinoshita et al., 2014). The LITA had a longer length, relative to the RITA, when compared to 4 out of 5 coronary artery types; the only exception was the AICA which had the smallest sample size out of all vascular conduits. The length difference between the LITA and RITA, although negligible, is an important factor in which each coronary artery conduit can anastomose (Weiss et al., 2013). The LITA is usually most favoured because of its close proximity to the heart (Berdajs and Turina, 2011). The RITA may be considered for arteries like the PICA in instances where it is sufficiently long (González Santos et al., 2005), which was not the case for most of the comparisons.

The mean wall thickness of the RITA is 87.9±15.35 um while the LITA has a mean thickness of 86.07±18.28 um. The LITA and RITA have mean wall thicknesses similar to the AICA and LCX which have values of 82.80±15.76 cm and 80.90±17.97 cm, respectively. Wall thicknesses that are similar are important since they reduce the risk of intimal hyperplasia (Sur et al., 2014). Most of the studies do not focus on wall thickness as an isolated component but rather the permeability of the graft as the main factor contributing to patency (Martínez-González et al., 2017).

The mean diameters of the LITA and RITA are closely related to almost all coronary arteries. The mean difference ranged between -0.01 cm to 0.38 cm. The two conduits are very similar to the LCX and the AICA, and this was indicated by an difference (net difference) close to zero. The LITA is also close in diameter to the PICA and the RCA, to the extent that other conduits are not. The reasonable expectation is that the LITA and RITA have the parameters that make them both equally suitable (Taggart et al., 2019, Fukui, 2019). However, there are studies looking to establish the superiority of using both ITAs as opposed to one (Sef and Raja, 2021).

The LITA has been traditionally preferred over the RITA despite their similar morphology (Lytle, 2013). Most surgeons in the survey shared a similar sentiment, even going as far as indicating that the use of both arteries might be unfavourable, this sentiment was shared by surgeons in a study by Jayakumar et al., 2019. It was only the least experienced surgeons that seemed open to the idea of a bilateral anastomosis, which affirms studies that have shown that the technique is still in its early stages and the superiority of both has not been evident (Sef and Raja, 2021).

Almost all respondents in the survey indicated their preference of the SV over the RITA, especially in emergency situations.

5.2.2. THE SAPHENOUS VEIN AND RADIAL ARTERY

Each time the SV was compared to all the coronary arteries it generally had a longer length. This confirms what has been reported in literature about SV's length playing a major role in the development of anastomotic and suturing techniques (Favaloro et al., 1970, Caliskan et al., 2020). The length difference between the SV and other coronary arteries allows room for some degree of manipulation, which is advantageous for certain sequential techniques (Sabik III, 2011).

The mean wall thickness of the SV is 127.97±34.99 um. Other studies have shown the wall thickness to range from 143 ± 32 um to 291 ± 35 um (ÜnlÜ et al., 2003). Compared to most coronary arteries, the SV seems to have a bigger wall thickness. While the SV graft is less prone to intimal hyperplasia (Sur et al., 2014), the mismatch in wall thickness is one of the factors contributing to SV graft failure (Xenogiannis et al., 2021).

The mean diameter of the SV is closely related to the RCA, LCX, PICA and AICA. This indicates the potential versatility of the SV graft, especially in emergency situations. Most surgeons indicated sole or complementary use of the SV graft for frail patients. The combined use of the LITA and SV is often supported in literature for multivessel grafts (Schwann et al., 2013).

The RA in all comparisons had the second lowest mean length difference, indicating the RA as always being longer than all coronary arteries. This is one of the reasons why most debates around the use of arterial versus venous grafts tend to involve the RA and the SV (Al-Sabti et al., 2013). The RA is often preferred because of its easier handling (Martínez-González et al., 2017, Verma et al., 2004). However, none of the surgeons selected the RA as either one of their most used or least used arteries. This may be due to lack of evidence about its superiority to the SV graft (Schwann et al., 2017).

The mean histological thickness of the RA is 100.83±25.32. This was markedly higher than other conduits. However, unlike the SV the RA has more SMC in its tunica media – which makes it even more prone to vasospasms compared to other arterial grafts (Barner, 2013).

5.2.3. THE INFERIOR EPIGASTRIC AND RIGHT GASTRO-EPIPLOIC ARTERY

The RGEA and IEA have histological wall thickness and length indices that are similar to the LITA and RITA when compared with the RCA, LCA, AICA and PICA. Some studies have shown evidence of the similarity of the RGEA to both ITA (Suma, 2016). Apart from having a similar morphology, it also can be treated in the same way since it may be anastomosed *in-situ* (Pym, 2006). Since the RITA often relies on length to successfully anatomize the PICA, the RGEA is an alternative since it is closer to the coronary artery.

Most surgeons did not consider the RITA in isolation, with only 1 out of 3 indicating the occasional use. In all instances, none of the respondents indicated the RGEA as an alternative. This might be because the RGEA and IEA are not grafts that have been traditionally used (Buche et al., 1992, Barner, 2013).

The morphological variation of coronary artery length was not affected by sex and age, or no visible trend was observed; the only patterns in mean differences were found between this study and other studies in the literature review. The variation of diameters is affected by sex, age and the presence of a pathology, since coronary angiograms without CAD differed from those with the condition. Diameter and wall thickness are the prevalent factors that affect patency while length contributes to a conduit's suitability due to easier handling perioperatively, and lessened graft tension post operatively.

5.2.4. STUDY LIMITATIONS AND POTENTIAL FOR FUTURE STUDIES

The mean age of the body cohort was relatively higher than the coronary angiogram cohort and this could have created discrepancies in the results since age plays a major role in cellular integrity. Sex was also skewed for both populations, with the coronary angiogram repository having relatively more men as opposed to women. The opposite was true in the body population. Furthermore, although inter-person validity for the angiograms was conducted by a professional radiologist, 2D imaging is not the most suitable for measuring since foreshortening can occur.

There is no information regarding the cause of death for the body cohort which caused a limitation, similarly information about the treatment of patients with CAD was not available. There is a grey area about the patency of other arterial grafts as opposed to the LITA and RITA, primarily due to the retrospective nature of the study. Most studies rely on reviewing literature as opposed to investigations that are prospective in nature. These prospective investigations have only been done in relation to the SV, LITA and RA.

Comparisons between the body cohort and the coronary angiograms did not take into account the impact of tissue processing on the vessels obtained from the bodies. This possess a further limitation. The survey responses were relatively low when compared to other studies. For future studies a project that is conducted over a longer period of time, involving live patients would shed more light of the patency of grafts including taking into account the lived experiences of surgeons.

CHAPTER 6: CONCLUSION

This study provided a uniquely South African perspective. The finds show that variations in morphology are not based on sex or age but geographical location. According to the quantitative data, the LITA and RITA are the most similar vascular conduits in comparison to coronary arteries. Both arterial grafts are also similar to one another which may be an advantage for bilateral anastomosis. However, due to the length and location of the RITA, the SV tends to take preference over the RITA. The SV is also a consistently long vessel when compared to coronary arteries. In addition, it is situated superficially which makes it easily accessible.

This is an important consideration for surgeons especially in emergencies. Furthermore, most consultants are prone to working with training surgeons and responsibility of teaching might make the SV a popular choice as opposed to the RITA which may require more complex procedures such as skeletonization.

The RA shares a similar morphology with the SV. However, both vessels are more likely to be mismatched with the coronary arteries which can result in hyperplasia; and there are relatively fewer reports of RA graft failure as a result of handling. The RGEA and IEA share the same similarity as the ITA, from a quantitative perspective, when compared to some coronary arteries. The RGEA has an advantage over the RITA because of its close proximity to the PICA. The IEA might be an option in multivessel grafting because of its inability to be grafted in-situ like the RITA, LITA while the RGEA leaves it at a disadvantage.

In conclusion, this investigation shows that the LITA is the most suitable vascular conduit in terms of morphological characteristics, location, and surgeon preference. More work needs to be done to assess the patency of arterial versus venous grafts, although the SV is the second most suitable graft if the right harvest and grafting techniques are used. The third most suitable vascular conduit is the RA, since it is the second longest graft (or longest arterial graft) which allows for easier handling, although more investigations are needed to quantify its propensity for vasospasms. The fourth and fifth most suitable grafts are the RITA and the RGEA. The RITA has a greater advantage over the RGEA due to its similarity to the LITA. The only disadvantage is the fact that it may have an insufficient length. The RITA is still a better conduit since it can work on various coronary arteries, and not just the PICA. More investigations are needed to assess the effects of using the ITA bilaterally. The IEA is the least suitable vascular conduit. It is not eliminated solely because of morphology but its location seems to hinder its accessibility and potential use.

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8. APPENDICES

8.1. SURVEY

Section A: Informed consent and study synopsis

Section B: Demographic Questionnaire Below is a set of questions asking you to tell us a bit about yourself. Please attempt to answer as accurately as possible. Please note personal details like the participant's name and affiliated hospital/institution will be anonymised as per the consensual agreement in the first section of this survey.

B1. Please provide your name and surname.

B2. Please indicate the name of the hospital/institution that you are affiliated with.

B3. Which of the following best describes the hospital/institution that you are affiliated with.

Private sector/Public sector

Please indicate the name of your role within the hospital/institution mentioned above.

B5. Which of the following best describes your role.

Registrar/Senior registrar

B6. How many times on average do you perform CABG surgery in a calender year?

Less than 5

Less than 10

More than 10

B7. How long have you been conducting CABG surgery in terms of years (at least once every year)?

Less than 12 months

Less than 5 years

More than 5 years, but less than 10 years

More than 10 years, but less than 20 years

More than 20 years

Section C: Frequency of conduit(s) used in CABG You may select more than one option.

C1. Which of the following do you regularly use (i.e. several times within a year)?

Please tick all appropriate boxes (listed in alphabetical order).

Gastroepiploic Artery

Inferior Epigastric Artery

Left Internal Mammary Artery (LIMA)

Radial Artery

Right Internal Mammary Artery (RIMA)

Saphenous Vein

C2. Which of the following would you feel comfortable using if only a few times a year? Please tick all appropriate boxes (listed in alphabetical order).

Gastroepiploic Artery

Inferior Epigastric Artery

Left Internal Mammary Artery (LIMA)

Radial Artery

Right Internal Mammary Artery (RIMA)

Saphenous Vein

Section D: Conduit suitability under different clinical scenarios

D1. In a typical low risk patient in whom you plan 3 – 4 distal anastomoses and who has good left ventricular function, how important is it to you to use bilateral mammary arteries for grafting? 1 = least important; 10 = most important

D2. In a typical patient as described above, how important is it to you to skeletonise your mammary vessels? 1 = least important; 10 = most important

D3. In a typical patient as described above, how important is it to you for each graft to serve only one distal anastomosis rather than sequential, T or Y configurations? 1 = least important; 10 = most important.

D4. In a frail patient with comorbidities, would your practice (as stated in Q3 – Q6) change? If yes, how?

D5. In a typical low risk patient in whom you plan 3 – 4 distal anastomoses and who has good left ventricular function, how important is it to you to use all arterial grafts? 1 = least important; 10 = most important.

D6. A patient undergoing PCI in the cath lab is brought for emergency surgery. Would your practice (as stated in Q3 – Q6) change? If yes, how?

Section E: Other factors that may affect conduit choice

E1. Please allocate to each of the following considerations a number of points based on its importance in affecting your choice of conduit. You have a total of 10 points available and can choose to distribute it amongst the factors below (listed in alphabetical order). 0 points = no effect on decision; 10 points = only factor mentioned affecting decision. Please ensure the total number of allocated points adds up to, but does not exceed 10.

High quality evidence in literature

Patient choice

The competency of surgeon/practitioners harvesting the conduit

Theatre time available

To provide a training opportunity

Your experience in the approach

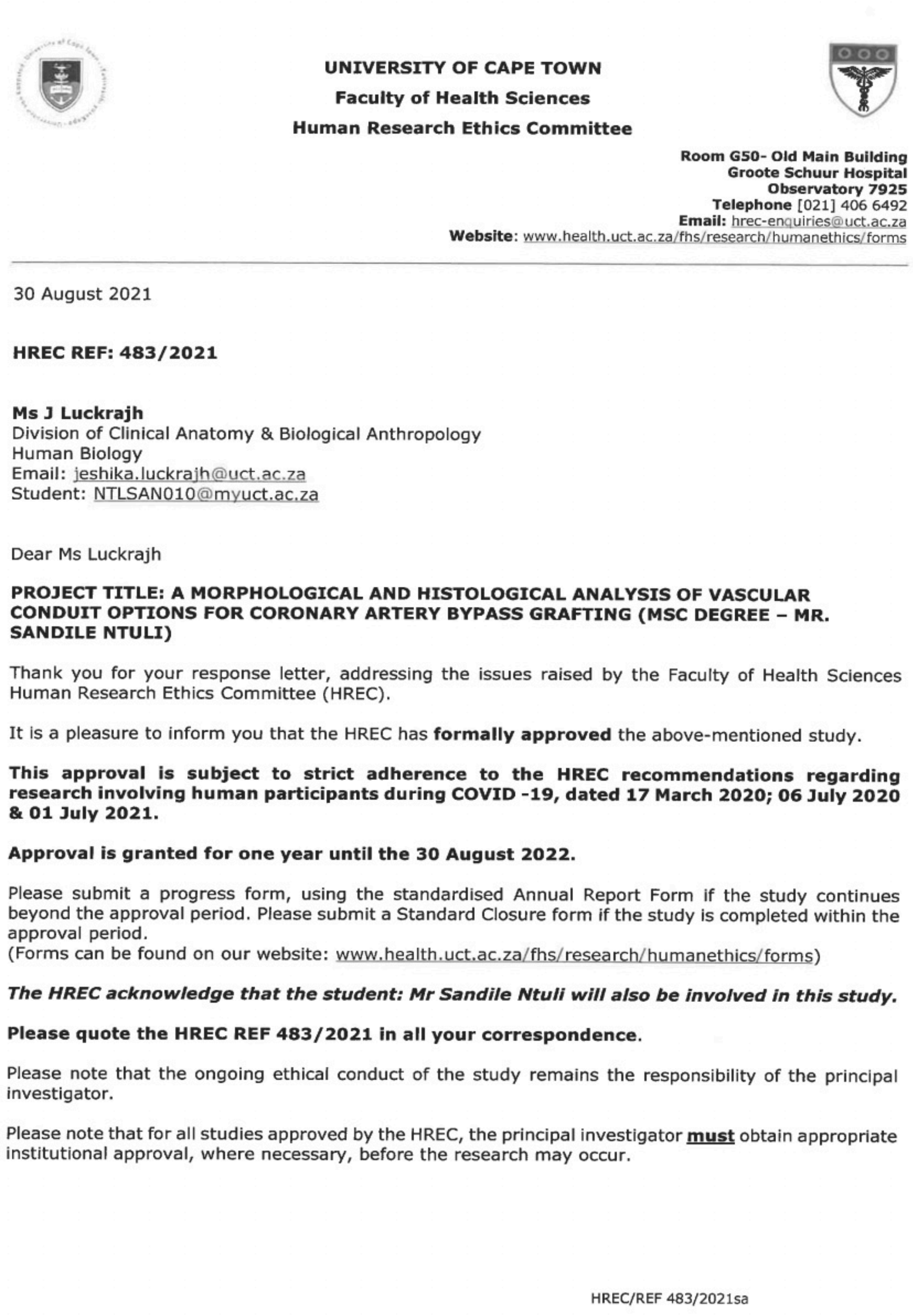
E2. In a typical patient as described above, please rank your preference for method of harvesting the great saphenous vein in order of preference (1 = most preferred, 3 = least preferred, 5 = never used)

E3. What is your preferred method of vein harvesting? Open harvesting Endoscopic vein harvesting (EVH) Bridging technique

E4. Do you have any other comments?

You have come to the end of the survey. Your participation is appreciated!

8.2 ETHICAL APPROVAL



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30 August 2021

HREC REF: 483/2021

Ms J Luckrajh
Division of Clinical Anatomy & Biological Anthropology
Human Biology
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Student: NTLSAN010@myuct.ac.za

Dear Ms Luckrajh

PROJECT TITLE: A MORPHOLOGICAL AND HISTOLOGICAL ANALYSIS OF VASCULAR CONDUIT OPTIONS FOR CORONARY ARTERY BYPASS GRAFTING (MSC DEGREE – MR. SANDILE NTULI)

Thank you for your response letter, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020; 06 July 2020 & 01 July 2021.

Approval is granted for one year until the 30 August 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Mr Sandile Ntuli will also be involved in this study.

Please quote the HREC REF 483/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC/REF 483/2021sa

8.3. Sample power Analysis

Univariate Analysis of Variance for Coronary Angiograms

Between-Subjects Factors			
		Value Label	N
Sex	1	Male	80
	2	Female	25

Descriptive Statistics			
Dependent Variable: RCA diameter			
Sex	Mean	Std. Deviation	N
Male	.2593	.08954	80
Female	.2698	.07176	25
Total	.2618	.08543	105

Tests of Between-Subjects Effects							
Dependent Variable: RCA diameter							
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter
Corrected Model	.002[a]	1	.002	.289	.592	.003	.289
Intercept	5.332	1	5.332	725.581	<.001	.876	725.581
Sex	.002	1	.002	.289	.592	.003	.289
Error	.757	103	.007				
Total	7.955	105					
Corrected Total	.759	104					

Tests of Between-Subjects Effects	
Dependent Variable: RCA diameter	
Source	Observed Power[b]
Corrected Model	.083
Intercept	1.000
Sex	.083

a. R Squared = .003 (Adjusted R Squared = -.007)

b. Computed using alpha = .05

Univariate Analysis of Variance for Body Cohort

Between-Subjects Factors			
		Value Label	N
Sex	1	Male	15
	2	Female	19

Descriptive Statistics			
Dependent Variable: RCA diameter			
Sex	Mean	Std. Deviation	N
Male	.3391	.09485	15
Female	.3413	.08766	19
Total	.3403	.08950	34

Tests of Between-Subjects Effects							
Dependent Variable: RCA diameter							
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter
Corrected Model	4.240E-5[a]	1	4.240E-5	.005	.943	.000	.005
Intercept	3.880	1	3.880	469.838	<.001	.936	469.838
Sex	4.240E-5	1	4.240E-5	.005	.943	.000	.005
Error	.264	32	.008				
Total	4.202	34					
Corrected Total	.264	33					

Tests of Between-Subjects Effects	
Dependent Variable: RCA diameter	
Source	Observed Power[b]
Corrected Model	.051
Intercept	1.000
Sex	.051

a. R Squared = .000 (Adjusted R Squared = -.031)

b. Computed using alpha = .05

8.4 MEASUREMENT BODY COHORT

Table Number	Sex	Age	LENGTH1	LENGTH2	D1	LENGTH12	LENGTH23	D15	LENGTH113	LENGTH214	D116	LENGTH124	LENGTH225	D127	LENGTH135	LENGTH236	D138
1	F	81	12.4	12.35	0.263333333	2.1	1.533333	0.296666667	6.55	7.533333	0.213333333	0	0	0	5.033333333	5.2	0.816666667
2	M	92	10	10.53333	0.363333333	2.9	1.666667	0.29	10.3	10.51667	0.236666667	12.83333333	11.33333	0.27	9.843333333	0	0.17
3	M	80	11.43333333	11.45	0.376666667	0	0	0	0	0	0	0	0	0	7.383333333	7.633333	0.216666667
4	M	69	12.33333333	12.8	0.32	1.883333333	1.796667	0.216666667	8.933333333	9.083333	0.243333333	0	0	0	5.466666667	5.4	0.15
5	M	54	12.5	12.8	0.25	1.55	1.393333	0.293333333	8.366666667	8.283333	0.161666667	18.33333333	19.11667	0.26	3.766666667	4.05	0.091666667
6	M	77	12.45	12.53667	0.266666667	1.133333333	1.25	0.328333333	7.75	7.893333	0.183333333	13.93333333	14.28333	0.175	4.683333333	4.973333	0.113333333
7	F	64	11.43333333	11.69	0.313333333	1.25	1.331667	0.233333333	0	0	0	9.05	0.286667	0.286666667	8.8	8.806667	0.073333333
8	M	82	12.63333333	11.45	0.363333333	1.383333333	1.6	0.38	7.336666667	7.183333	0.146333333	16.8	17.85	0.094666667	5.383333333	6.2	0.196666667
9	M	92	10.6	11.81667	0.38	0.596666667	0.841667	0.253333333	5.6	5.35	0.184666667	14.01666667	14.46667	0.173333333	8.403333333	9.033333	0.21
10	F	67	17.2	16.46667	0.291666667	0.846666667	1.1	0.3	5.866666667	6.183333	0.14	12.88333333	13.05	0.301666667	6.15	6.4	0.106666667
11	M	93	0	0	0	0.84	1.116667	0.31	9.833333333	10.15	0.286666667	15.46666667	15.95	0.201666667	7.15	7.466667	0.196666667
12	F	88	13.08333333	13.38333	0.223333333	0.78	0.916667	0.228333333	9.533333333	9.983333	0.196666667	13.99	14.43	0.293333333	7.833333333	8.016667	0.181666667
13	M	81	20.53333333	20.61667	0.3	1.15	1.183333	0.356666667	9.666666667	10.07333	0.226666667	15.89666667	16.09333	0.296666667	4.39	4.433333	0.516666667
14	F	83	14.33333333	15.17667	0.35	0.91	0.926667	0.29	9.533333333	10.12333	0.186666667	7.116666667	7.123333	0.31	5.916666667	6.15	0.25
15	F	74	16.43333333	19.9	0.326666667	1.066666667	1.056667	0.303333333	6.623333333	8.366667	0.193333333	14.36666667	17.00667	0.206666667	3.966666667	5.116667	0.166666667
16	M	84	10.13333333	10.25	0.266666667	1.033333333	1.563333	0.28	5.283333333	6.25	0.2	11.01666667	12.03333	0.206666667	3.533333333	3.866667	0.113333333
17	M	64	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	M	91	8.016666667	8	0.173333333	0.823333333	0.95	0.416666667	6.2	6.553333	0.25	13.63333333	15.23333	0.28	0	0	0

19	**F**	**86**	12.15	12.41667	0.25	0.883333333	0.95	0.32	11.61333333	11.86667	0.273333333	11.39	11.55	0.236666667	7.5	7.666667	0.253333333
20	**F**	**74**	9.616666667	9.883333	0.253333333	0	0	0	11.66666667	12.5	0.216666667	11.73333333	12.1	0.286666667	5.933333333	6.116667	0.21
21	**F**	**98**	11.56666667	11.26667	0.366666667	1.566666667	1.9	0.3	7.066666667	7.4	0.2	11.23333333	10.9	0.166666667	7.466666667	7.8	0.133333333
22	**F**	**68**	7.6	7.7	0.283333333	1.8	1.966667	0.266666667	4.233333333	5.4	0.183333333	12.23333333	12.63333	0.266666667	8.266666667	9.033333	0.116666667
23	**F**	**67**	9.5	9.966667	0.316666667	1.266666667	1.266667	3	8.5	8.466667	0.466666667	10.2	9.966667	0.7	4.766666667	4.966667	1.333333333
24	**F**	**81**	6.233333333	6.466667	0.466666667	1.033333333	1.666667	0.566666667	6.116666667	5.7	0.316666667	11.15	11.83333	0.366666667	8.7	8.566667	0.266666667
25	**F**	**74**	9.9	10.3	0.483333333	1.55	1.35	0.483333333	7.733333333	7.8	0.22	0	0	0	5.233333333	6.333333	0.183333333
26	**M**	**79**	9.4	9.266667	0.4	1.1	1.283333	0.5	6.6	6.766667	0.2	12.46666667	12.4	0.266666667	8.433333333	8.366667	0.15
27	**F**	**77**	14.5	14.93333	0.326666667	1.316666667	1.233333	0.583333333	4.9	8.433333	0.173333333	11.86666667	14.06667	0.2	6.233333333	6.533333	0.666666667
28	**F**	**80**	4.6	5.333333	0.5	1.6	1.6	0.516666667	10.9	11	0.383333333	12.66666667	12.81667	0.266666667	4.7	5.533333	0.116666667
29	**F**	**89**	0	0	0	1.583333333	1.5	0.366666667	11.6	12.2	0.3	0	0	0	4.433333333	5.733333	0.266666667
30	**F**	**56**	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	**M**	**58**	4.766666667	4.566667	0.25	1.133333333	1.166667	0.45	3.7	4.066667	0.77	14.6	14.8	0.303333333	0	0	0
32	**F**	**66**	3.524074074	3.577778	0.17	1.3	1.4	0.4	9.133333333	9.6	0.233333333	0	0	0	4.666666667	22.26667	1.966666667
33	**F**	**105**	10.51666667	10.7	0.48	1.133333333	1.233333	0.533333333	4.603333333	4.316667	1.383333333	10.66666667	12.4	2.333333333	7.566666667	7.916667	0.223333333
34	**F**	**72**	8.7	8.666667	0.416666667	0.533333333	0.513333	0.313333333	7.4	9.6	0.283333333	11.61666667	11.4	0.246666667	5.9	6.1	0.833333333
35	**F**	**64**	10.63333333	11.7	0.35	1.3	1.2	0.433333333	8.666666667	9.233333	0.22	10.66666667	10.8	0.3	6.466666667	6.666667	2.3
36	**M**	**64**	10.96666667	11.86667	0.35	2.133333333	1.866667	0.7	4.333333333	6.866667	0.333333333	12.6	13.26667	0.266666667	0	0	0
37	**M**	**65**	11.36666667	11.2	0.5	1.533333333	1.7	0.6	5.833333333	6.233333	1.15	10.6	9.333333	0.283333333	7.066666667	7.8	0.166666667
38	**M**	**87**	14.55	15	0.533333333	2.933333333	3.1	0.633333333	6.7	9.7	0.3	17.6	19.56667	0.316666667	5.566666667	5.8	0.633333333
39	**M**	**84**	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	**F**	**48**	13.5	13.53333	0.253333333	0.716666667	0.816667	0.32	11.618	0	0	15.36666667	15.41667	0.353333333	3.466666667	3.783333	0.196666667

8.5 SIMILARITY TABLE

TABLE No.	RCA-L	RCA-D	RITA-L	RITA-D	LITA-L	LITA-D	RA-L	RA-D	RGEA-L	RGEA-D	IEA-L	IEA-D	SV-L	SV-D
9	10.6	0.4	-3.8	0.2	-6.7	0.2	-12.5	0.1			-4.4	0.3		
10	17.2	0.3	1.8	0.1	1.8	0.1	-4.9	0.1	-0.1	0.0	-3.9	0.2		
13	20.5	0.3	7.2	0.1	2.4	0.1	-2.0	0.1	6.3	0.1				
15	16.4	0.3	0.0	0.2	3.4	0.1	-2.8	0.1	-5.0	0.1				
18	8.0	0.2	-9.0	-0.1	-6.0	0.0			-9.8	0.1	-8.1	0.1	-27.3	-0.1
20	9.6	0.3			-9.7	-0.1	-12.6	0.0	-12.3	0.0			-21.1	-0.2
22	7.6	0.3			-7.9	0.1			-8.7	0.1	-8.9	0.2	-31.1	0.1
23	9.5	0.3			-4.6	-1.5	-14.3	0.0			-7.7	-0.7	-30.3	-0.4
24	6.2	0.5	-5.5	0.2	-9.1	0.2	-14.7	0.3	-11.5	-0.4			-27.1	0.2
26	9.4	0.4			-9.4	0.2	-14.0	0.2	-5.9	0.4	-1.4	0.2	-15.9	0.1
28	4.6	0.5	-11.2	-2.0	-12.1	0.3	-18.9	0.2	-7.0	0.2	-10.1	-1.3	-22.4	0.3
31	4.8	0.3			-10.5	0.1								
34	8.7	0.4	-7.4	0.2									-23.1	0.2
37	11.4	0.5	-3.9	0.1	-4.9	0.3			-9.9	0.2	-0.1	0.3		
38	14.6	0.5			-7.4	0.3	-9.0	0.2			-0.3	0.3	-13.1	0.3

TABLE No.	LCA-L	LCA-D	RITA-L	RITA-D	LITA-L	LITA-D	RA-L	RA-D	RGEA-L	RGEA-D	IEA-L	IEA-D	SV-L	SV-D
1	2.1	0.3	-16.4	0.1	-15.3	0.0								
10	0.8	0.3	-14.6	0.1	-14.6	0.1	1.0	0.1	-16.5	0.0	-20.2	0.2		
12	0.8	0.2			-17.2	-0.1	-17.1	0.0					-24.0	0.0
14	0.9	0.3	-14.7	0.2	-15.3	0.1	-19.4	0.1			-12.7	0.1	-35.9	0.0

15	1.1	0.3	-13.5	0.1	-12.0	0.1	-18.2	0.0	-20.4	0.1				
21	1.6	0.3	-13.1	0.1	-12.1	0.1	-18.1	0.2	-9.1	0.0				
22	1.8	0.3			-13.7	0.1			-14.5	0.0	-14.7	0.2	-36.9	0.1
23	1.3	3.0			-12.8	2.8	-22.5	2.7			-15.9	2.0	-38.6	2.3
24	1.0	0.6	-10.7	0.4	-14.3	0.3	-19.9	0.4	-16.7	0.2			-32.3	0.3
26	1.1	0.5			-17.7	0.3	-22.3	0.3	-14.2	0.3	-9.7	0.3	-24.2	0.2
33	1.1	0.5	-13.6	0.3	-11.9	0.3	-19.8	0.3	-20.2	0.4				
34	0.5	0.3	-15.5	0.1									-31.3	0.1
36	2.1	0.7			-18.7	0.6					-15.7	0.5	-38.2	0.3
37	1.5	0.6	-13.8	0.2	-14.8	0.4			-19.7	0.3	-9.9	0.4		
38	2.9	0.6			-18.0	0.4	-20.6	0.3			-11.9	0.4	-24.7	0.4
40	0.7	0.3	-18.8	0.1	-21.8	0.1	-22.7	0.0					-38.0	0.2

TABLE No.	**LCX-L**	**LCX-D**	**RITA-L**	**RITA-D**	**LITA-L**	**LITA-D**	**RA-L**	**RA-D**	**RGEA-L**	**RGEA-D**	**IEA-L**	**IEA-D**	**SV-L**	**SV-D**
5	8.4	0.2			-13.7	0.0			-11.2	0.0			-35.0	-0.3
8	7.3	0.1	-8.1	0.0	-5.9	-0.1	-14.6	-0.1	-18.3	-0.1				
9	5.6	0.2	-8.8	0.0	-11.7	0.0	-17.5	0.0			-9.7	0.1		
10	5.9	0.1	-9.6	-0.1	-9.5	-0.1	-16.2	0.0	-11.5	-0.2	-15.2	0.0		
16	5.3	0.2	-13.4	0.0	-13.7	-0.1	-18.7	0.2			-11.8	-0.1		
18	6.2	0.3	-10.9	0.0	-7.8	-1.4			-11.6	0.1	-9.9	0.1	-29.1	0.0
22	4.2	0.2			-11.3	0.0			-12.1	0.0	-12.2	0.1	-34.5	0.0
23	8.5	0.5			-5.6	-1.4	-15.3	0.1			-8.7	0.4	-31.3	-0.3
24	6.1	0.3	-5.6	0.0	-9.3	0.1	-14.8	0.2	-11.2	0.0			-27.2	0.1
27	4.9	0.2	-8.8	-0.1	-8.6	-0.1	-17.6	-0.1	-21.2	-0.2			-31.2	0.0

28	10.9	0.4	-4.9	-2.0	-5.8	0.2	-12.6	1.1	-0.7	0.1	-3.8	0.2	-16.1	0.1
29	11.6	0.3	-3.2	0.0	-3.0	-0.2	-9.7	0.1			-2.8	0.2	-28.2	0.1
33	4.6	1.4	-10.1	1.1	-8.4	1.3	-16.3	0.9	-16.8	1.2				
34	7.4	0.3	-8.7	0.0									-24.4	0.1
36	4.3	0.3			-16.5	0.2					-13.5	0.1	-36.0	-0.1
37	5.8	1.2	-9.5	0.8	-10.5	0.9			-15.4	0.8	-5.6	0.9		

TABLE No.	**AICA-L**	**AICA-D**	**RITA-L**	**RITA-D**	**LITA-L**	**LITA-D**	**RA-L**	**RA-D**	**RGEA-L**	**RGEA-D**	**IEA-L**	**IEA-D**	**SV-L**	**SV-D**
5	18.33	0.26			-3.70	0.04			-1.24	0.13			-25.03	-0.18
7	9.05	0.29	-5.45	0.08			-9.20	0.11			-6.52	0.11	-27.19	0.01
8	16.80	0.09	1.40	-0.06	3.57	-0.15	-5.10	-0.19	-8.87	-0.16				
14	7.12	0.31	-8.51	0.18	-9.11	0.12	-13.15	0.66			-6.47	0.16	-29.69	0.04
38	17.60	0.32			-3.33	0.09	-6.30	-0.18			2.77	0.05	-10.07	0.05

TABLE No.	**PICA-L**	**PICA-D**	**RITA-L**	**RITA-D**	**LITA-L**	**LITA-D**	**RA-L**	**RA-D**	**RGEA-L**	**RGEA-D**	**IEA-L**	**IEA-D**	**SV-L**	**SV-D**
1	5.03	0.82	-13.45	0.60	-12.39	0.54								
2	9.84	0.17	-7.24	0.00	-8.08	-0.01	-13.79	-0.06	-8.61	-0.08	-7.13	-0.05	-26.84	-0.13
5	3.77	0.09			-18.26	-0.12			-15.80	-0.04			-39.59	-0.34
7	8.80	0.07	-5.70	-0.14			-9.45	0.31			-6.77	-0.11	-27.45	-0.21
9	8.40	0.21	-6.03	0.02	-8.87	0.04	-14.65	-0.11			-6.90	0.10		
12	7.83	0.18			-10.18	-0.11	-10.02	-0.14					-16.97	-0.08
13	4.39	0.52	-8.94	0.29	-13.71	0.28	-18.14	0.00	-9.81	0.33				
15	3.97	0.17	-12.50	0.01	-9.11	-0.05	-15.26	-0.13	-17.48	-0.07				
16	3.53	0.11	-15.15	-0.07	-15.48	-0.15	-20.44	-0.17			-13.52	-0.18		
19	7.50	0.25	-7.77	0.03	-9.58	0.08	-12.21	0.04	-8.02	0.08	-6.17	0.19	-18.71	0.02

21	7.47	0.13	-7.15	-0.05	-6.19	-0.09	-12.24	0.00	-3.20	-0.19				
22	8.27	0.12			-7.23	-0.08			-8.06	-0.10	-8.20	0.04	-30.43	-0.06
24	8.70	0.27	-3.03	-0.04	-6.66	0.02	-12.27	1.84	-9.03	-0.08			-24.63	0.05
26	8.43	0.15			-10.34	-0.09	-14.94	1.72	-6.84	-0.07	-2.37	-0.04	-16.84	-0.14
29	4.43	0.27	-10.37	0.01	-10.14	-0.21	-16.84	0.03			-10.00	0.14	-35.37	0.05
32	4.67	1.97	-12.80	1.84							-5.39	1.82	-36.66	1.44
33	7.57	0.22	-7.13	-0.03	-5.48	0.03	-13.35	-0.20	-13.80	0.08				
38	5.57	0.63			-15.36	0.40	-17.93	-0.35			-9.26	0.37	-22.10	0.36
40	3.47	0.20	-15.68	0.01	-19.01	0.02	-19.90	-0.28					-35.24	0.05