AORTIC VALVE REPLACEMENT: ANATOMICAL CONSIDERATIONS IN A NARROW AORTIC ROOT

by

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Submitted in fulfillment of the requirements for the degree of

MASTER OF MEDICAL SCIENCES

In the Department of Clinical Anatomy,

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University of KwaZulu-Natal

South Africa

2015

To my family

The process of learning consists of 5 stages:

1. *Silence*
2. *Listening*
3. *Understanding*
4. *Remembering*
5. *Teaching others*

Old Jewish Proverb

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DECLARATION

This study represents original work by the author and has not been submitted in any other form to another University. Where the work of other people has been included, acknowledgement to this has been made in accordance to the text and references quoted.

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ACKNOWLEDGEMENT

The author wishes to express his utmost appreciation and gratitude to the following Institutions, individuals and departments for their direct or indirect support in the preparation of this dissertation:

- To God the almighty, for his wish to keep us alive each day of our lives, and for making this work possible.
- To my parents Jeremiah and Virginia Mushiwokufa, my brothers Lincoln, Christopher,Crispen, Ronnie, Tafadzwa and my sister Bernadette and their families for standing by me and believing in me in my times of need.
- My Supervisor, Professor K.S. Satyapal for the mentorship, inspiration, and guidance throughout this study
- My co-supervisors, Professor E.A. Vanker and Mrs L. Lazarus for the mentorship, inspiration, and guidance throughout this study
- University of Kwa-Zulu Natal and the Discipline of Clinical Anatomy for the academic support
- Dr S. Aiyer, Dr Pillay and the staff at Gale Street State Mortuary
- Amanda Chaukura, Sandra Chideme, Kelvin Chanaiwa for the love and encouragement
- My friends Torence Siduna, Blessed Ziyambe, Tapiwa Dhliwayo, Shingirayi Sibamba, Perseverance and Gerrard Mphisa for the love
- Professor Ben Sartorius and Mrs F Nkwanyana for their kind assistance with statistical consultation
- Dr Nasirudeen Ajayi, Mr Domnic Marera, Arishka Kalicharan, Shivanni Govender the rest of my collegues and staff of Clinical Anatomy (UKZN), for making the

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LIST OF ABBREVIATIONS

ABBREVIATION	INTERPRETATION
LCO	Left coronary ostium
RCO	Right coronary ostium
AVR	Aortic valve replacement
PPM	Patient-prosthesis mismatch
LAS	Left aortic sinus
RAS	Right aortic sinus
NCS	Non-coronary sinus
AA	Aortic annulus
SJ	Sino-tubular junction
EOAI	Effective valve orifice area index
PPM	Patient prosthesis mismatch
BSA	Body surface area

ABSTRACT

Coronary artery ostial stenosis is a life threatening complication of aortic valve replacement (AVR) surgery. It occurs in 3-5% of all AVR operations. Most cases occur 1 to 6 months following AVR. However, some cases have been recorded during and immediately after operation and these have been attributed to embolization of calcium debris, coronary artery spasm, occlusion by the prosthetic valve and distortion of the anatomy of the aortic root.

AVR is a standard procedure routinely performed to alleviate the symptoms of aortic valve stenosis and regurgitation. The standard procedure involves removing the diseased, poorly functioning valve cusps and implanting a mechanical or biological prosthesis whose size allows it to perform almost like a normal aortic valve. The size of the prosthesis may be determined through pre-operative echocardiographic assessment of the aortic root correlated to the body surface area of the patient. Intra-operative "sizing" of the aortic annulus is also performed using graduated obturators. The required size may not fit well in patients who have narrow aortic roots forcing the implantation of a smaller size prosthesis, a situation that is termed patient-prosthesis mismatch. To prevent patient-prosthesis mismatch surgeons have developed techniques to enlarge the aortic annulus and place larger prostheses. However, the operating surgeon may elect not to surgically enlarge the aortic annulus but forcibly implant or "shoe-horn" a larger prosthesis.

The aim of this study was to investigate and document anatomical changes on the aortic root when a large size valve is implanted in a simulated AVR operation where the aortic root is considered to be narrow. The study also aimed to report the size of the aortic root and the influence of sex, race, body height and age. Additionally, the study demonstrates the difference between the pliability of the aortic annulus and sino-tubular junction.

The study was conducted at Gale Street State Mortuary in Durban, KwaZulu-Natal, South Africa. A total number of 60 unfixed cadaveric heart specimens were selected for the investigations. For investigation of morphometry of the aortic root, 30 heart samples were selected for this study. The other 30 specimens were selected for the experimental study to investigate the effect of placing a large size valve. Ethics approval for the study was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Committee (Ethics number 307/15).

Of the 30 normal hearts, the mean aortic annulus diameter was 20.2mm and the mean sino-tubular junction diameter was 21.8mm. There was a significant correlation between aortic root diameters and age but no association with sex, race or body height. The mean diameter of the left coronary ostium (LCO) was 6.1mm. The most common shapes of the LCO were circular (96.7%) and ellipsoidal (3.3%). The mean distance of LCO from the aortic annulus was 12.6mm. The LCO was located below, on and above the sino-tubular junction in 73.3%, 23.3% and 3.3%, respectively. The study showed clearly that when an oversized prosthesis is implanted into a normal aortic root, the LCO is distorted and displaced caudally towards the aortic annulus. A transverse ridge of aortic tissue, in the form of a tight bar was created above the LCO extending from the adjacent commissures. The sino-tubular junction was more pliable than the aortic annulus by a factor of 1.5.

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

The aortic root represents the outflow tract of the left ventricle as it joins the aorta, providing a conduit for oxygenated blood to flow from the heart to the body (Anderson, 2000). Its functional anatomy has been described by anatomic dissection, echocardiography, ultrasonography, computer aided tomography, magnetic resonance imaging and coronary angiography. It is cylindrical and provides the supporting structure of the aortic valve and consists of aortic annulus, three cusps, aortic sinuses and the sino-tubular junction (Ho, 2009).

The aortic valve is a three cusped valve that ensures the unidirectional flow of blood from the left ventricle to the ascending aorta (Anderson, 2007). It accomplishes this by opening during systole to allow ejection of blood and closing during diastole to prevent backflow (Barret *et al.*, 2009). Any disease process that disrupts the integrity of the cusps and/or surrounding structures affects functionality of the valve, creating stenosis or insufficiency. Causes of aortic valve insufficiency include rheumatic fever, endocarditis, uncontrolled hypertension, aortic root dilatation and bicuspid valves (Kumar and Clark, 2010). Rheumatic fever, degenerative calcification, bicuspid and unicuspid valves have been implicated in aortic stenosis (Kumar and Clark, 2010).

Aortic Valve Replacement (AVR) has become a routine procedure in the treatment of aortic stenosis and insufficiency with over 200 000 operations being done worldwide annually (Brown *et al.*, 2009). The goal of AVR is to restore valve function, with the use of biologic or mechanical valves (David, 1999). Restoration of function is achieved by surgically replacing a correctly sized prosthesis that allows enough blood to be ejected during ventricular systole

(Standring *et al*., 2008). The size of prosthesis appropriate to the patient can be determined pre-operatively using pre-operation echocardiographic measurements of the aortic root correlated to the individual's body size viz. body surface area (BSA) (Castro *et al.*, 2002). Intra-operatively, the aortic annulus is "sized" using graduated obturators (Barret-Boyes, 1965). Aortic valve prostheses are available in the following sizes: 19 mm, 21 mm, 23 mm, 25 mm, 27 mm and 29 mm (Carpentier-Edwards, 2006). Small prosthetic valves can be obstructive, causing high pressure gradients between the left ventricle and aorta producing prosthesis-patient mismatch (David, 1999). Prosthesis-patient mismatch (PPM) was first described by Rahimtoola in 1978 as a phenomenon "present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve" (Dumesnil and Pibarot, 2011). To avoid PPM, the largest possible prosthesis should be implanted. However, this is not possible in patients with narrow aortic roots (David, 1999).

A narrow aortic root implies that the size of the prosthetic device used to replace the aortic valve is inadequate for the patient's physiological and functional requirements (Franco and Verrier, 2003). The surgical technique and size of prosthetic valve used depend on patient factors and surgeon's preferences (David, 1999). Surgeons have developed techniques to overcome PPM which can include mechanical dilatation with a Hegar's dilator (Bartels and Sievers, 1999), surgical aortic root enlargement (Nicks *et al.*, 1970; Manouguian and Seybold-Epting, 1979) and oblique valve placement (Ishida, 2001). In an attempt to insert a prosthesis (size matched to patient's BSA), in a patient with a narrow annulus, there could be significant PPM. In this situation, if the surgeon elects not to surgically enlarge the aortic root, the prosthesis would have to be forcibly implanted ('shoe horned') into the aortic root. This will produce distortion to the aortic root. This study was undertaken to elucidate the precise nature of the anatomic changes th at occur when implanting a disproportionately large prosthesis into a relatively narrow aortic root.

More recently, transcatheter aortic valve implantation (TAVI) is a technique that was developed as an alternative to AVR for patients who were deemed unsafe for major surgery (Cribier *et al*., 2002; Thomas and Mabin, 2012).

Coronary artery stenosis with associated reduction of blood flow to the myocardium is a life-threatening complication found in 5% of cases of AVR (Ziakas *et al.,* 2010) and 1% of TAVI cases (Ribeiro *et al*., 2013). It has been noted to occur during and i mmediately after surgery but mostly one to six months post operation (Pillai *et al.,* 2004 and Umran *et al.,* 2012). Coronary occlusion can occur when a prosthesis is implanted above the aortic annulus and sutures are placed along the scalloped shaped line of attachments for the native valve cusps (Ueda, 2010; Choi *et al*., 2013; Orihashi, 2013). Other causes of coronary artery stenosis are calcium debris embolization, occlusion by the prosthesis or oedematous reaction and ostial thrombosis due to trauma (Pillai *et al.,* 2004). Coronary artery spasm has also been reported to cause acute coronary blood flow blockage in patients undergoing AVR (Kinoshita *et al.,* 1991and Pragliola *et al.,* 2007).

1.2 SIGNIFICANCE OF THE STUDY

The object of this study is that an appropriate sized prosthesis can cause changes in the morphology and morphometry of the aortic root orifice, with special reference to the effect on the left coronary ostium (LCO). Coronary ostial obstruction has been reported more on the left than right coronary artery following both open surgery and TAVI. According to Ribeiro *et al*. (2013), the LCO is involved in 90% of coronary artery stenosis and it has been suggested that this could be related to the location of the LCO which is found lower than the right coronary ostium (RCO). The operating surgeon needs to know how a mismatched prosthetic valve can distort the anatomy of the aortic root with possible serious pathophysiological consequences. 'Shoe-horning' a large prosthesis into a narrow aortic root may appear to be simpler to the surgeon and requiring less time to perform, but the consequences could be serious. After an extensive literature review, no report was found detailing the anatomic effects of inserting a relatively large prosthesis into a narrow aortic root. As an additional study, we collected data in cadavers, correlating size of aortic root and LCO to race, sex, age and body height, in the absence of disease of the aortic valve.

1.3 AIM

The aim of this study was to investigate and document anatomical changes to the aortic root associated with mismatched AVR in a cadaveric model.

Research Objectives

1. To investigate the anatomical effects of a mismatched aortic valve prosthesis on:

i) The shape of the LCO.

ii) Alteration in the position of the LCO in relation to the valve ring.

iii) Distortion of the aortic wall above the coronary orifice.

2. To demonstrate the difference in pliability between the valve annulus versus the sino-tubular junction.
3. To investigate the influence of race, height and sex on the morphometry of the aortic root and LCO.

CHAPTER 2

LITERATURE REVIEW

2.1 THE AORTIC ROOT: HISTORICAL BACKGROUND

The earliest detailed study of the anatomy of the aortic valvular complex has been attributed to Leonardo da Vinci (1452-1519), who published descriptions and drawings of the heart chambers, valves and coronary vasculature (Figures 1 and 2) (Piazza *et al.,* 2008).

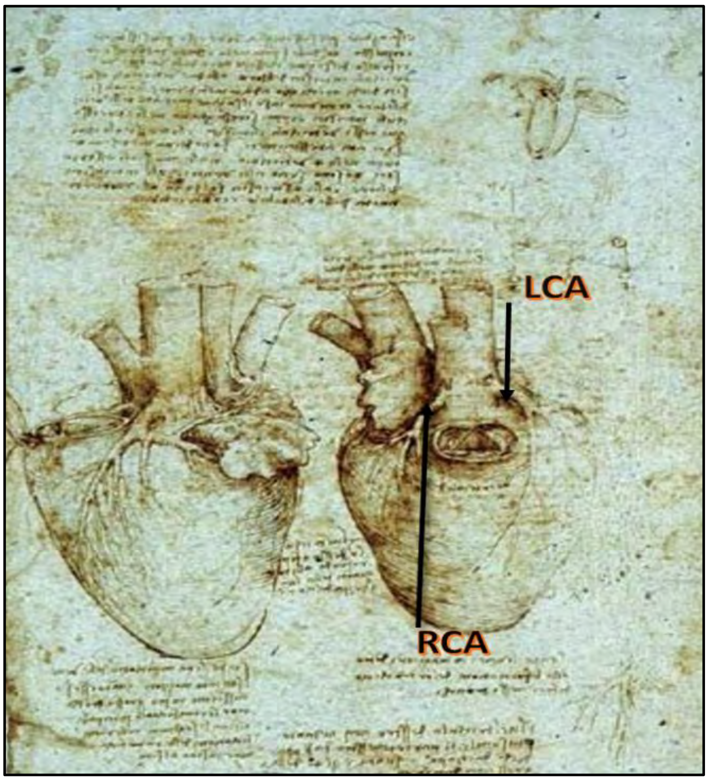

Figure 1: *Leonardo da Vinci's early sketches of the heart and coronary arteries (Adapted from Baumgartner, 1932)*

Key: **RCA** = Right coronary artery, **LCA** = Left coronary artery

However, a lack of understanding in the blood circulation meant that Leornado da Vinci could not reconcile his anatomic findings and the movement of blood in the heart (Tilea *et al.,* 2013).

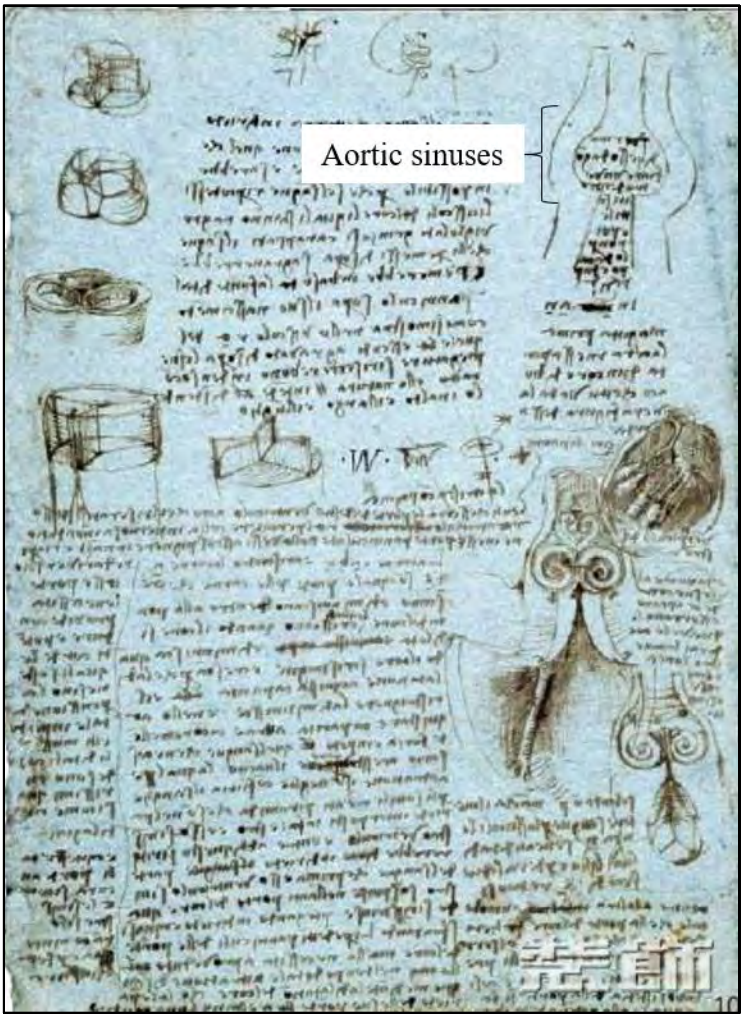

Figure 2*: An early sketch of the aortic valve by Leonardo da Vinci (Adapted from Clayton, 2012).*

The movement of blood within the cardiovascular system was first fully described by William Harvey (1578-1657) in 1628 (Aird, 2011). Despite these early advances in the study of cardiovascular anatomy and circulation, the structure of the aortic valvular complex remained a mystery for approximately 400 years (Clayton, 2012). The junction between the left ventricle and the ascending aorta was originally referred to as the “arterial ring” by anatomists but it was Freidrich G.J. Henle (1809-1885) who coined the term “aortic root” after realizing the complex nature of the aforementioned junction (Ho, 2009).

Given the ever increasing incidence of coronary artery disease, aortic valve disease and surgery there have been numerous investigations in the anatomy of the aortic root. With the advances in technology, the functional anatomy of the aortic root has been described by anatomic dissection, echocardiography, ultrasonography, computer aided tomography and magnetic resonance imaging (Anderson, 2000; Standring *et al*., 2008; Boon, 2009)

2.2 THE AORTIC ROOT: NOMENCLATURE OF AORTIC ROOT

For ease of reference, the terminology used throughout this dissertation is recorded in Table 1.

***Table 1**: Aortic root nomenclature*

Author (year)	Terminology	Terminologia Anatomica
Anatomical Terminology		
Standring *et al.* (2008)	Sinuses of Vasalva, Aortic sinus (right, left and non-coronary)	Sinus aortae
Standring *et al.* (2008)	Aortic valve leaflet (right, left and posterior)	Valvular coronaria (dextra, sinistra and non-coronaria respectively)
Standring *et al.* (2008)	Sino-tubular junction, sino-tubular ridge, supravalvular ridge	Crista supravalvularis
Clinical Terminology		
Townsend *et al*., (2004)	Aortic valve cusp (right, left and non-coronary)	Valvular coronaria (dextra, sinistra and non-coronaria respectively)

In the current thesis, the following anatomical terms will be used: (i) leaflets, (ii) right, left and non-coronary sinuses, (iii) anterior, right and left posterior leaflets, (iv) sino-tubular junction, and (v) inter-leaflet triangles.

2.3 THE AORTIC ROOT

2.3.1 GROSS ANATOMY

The aortic root is a continuation of the left ventricular outflow tract that extends to the sino-tubular junction where the ascending aorta begins (Anderson, 2000). In other words, the aortic root forms a bridge between the left ventricle and the ascending aorta (Tilea *et al.*, 2000).

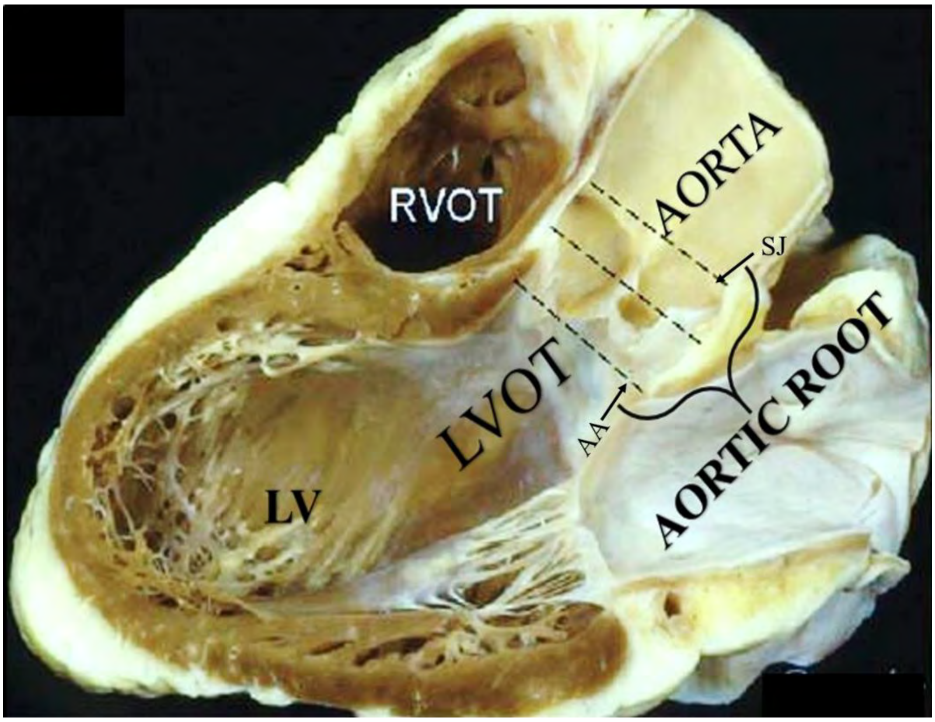

Figure 3*: A heart cut longitudinally through the left ventricle and aortic root. The left ventricular outflow tract continues as the aortic root which becomes the ascending aorta (Adapted from Ho, 2009).*

Key: RVOT = right ventricular outflow tract, **LVOT** = Left ventricular outflow tract, **LV** = Left ventricle

The aortic root is located at the centre of the heart and is related to all of its four chambers viz. right and left atria and right and left ventricles (Anderson, 2007; Ho, 2009). Furthermore, the aortic root is closely related to the subpulmonary infundibulum which is positioned anteriorly and to the left, and it lies between the orifices of the mitral and tricuspid valves (Anderson, 2000; Tilea *et al.*, 2013) (Figure 4).

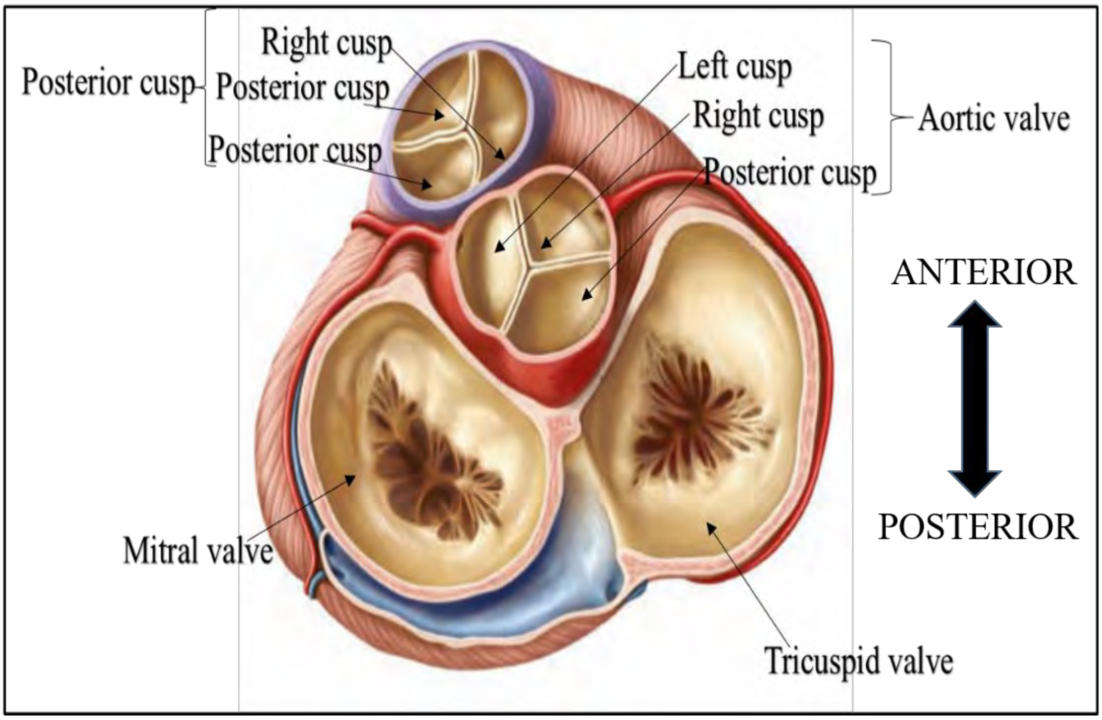

Figure 4: *Superior view of the heart showing the relationship of the aortic valve to the pulmonary, mitral and tricuspid valves. N.B. both atria have been removed.*
(Adapted from Gilroy et al., 2008)

The aortic root is also closely related to the atrioventricular node and the atrioventricular bundle (Anderson, 2007) (Figure 5). The wall of the aortic root is made up of the inner mucosal layer called tunica intima, medial muscular layer called tunica media and an outer pericardial layer called tunica externa (Butcher *et al.*, 2011).

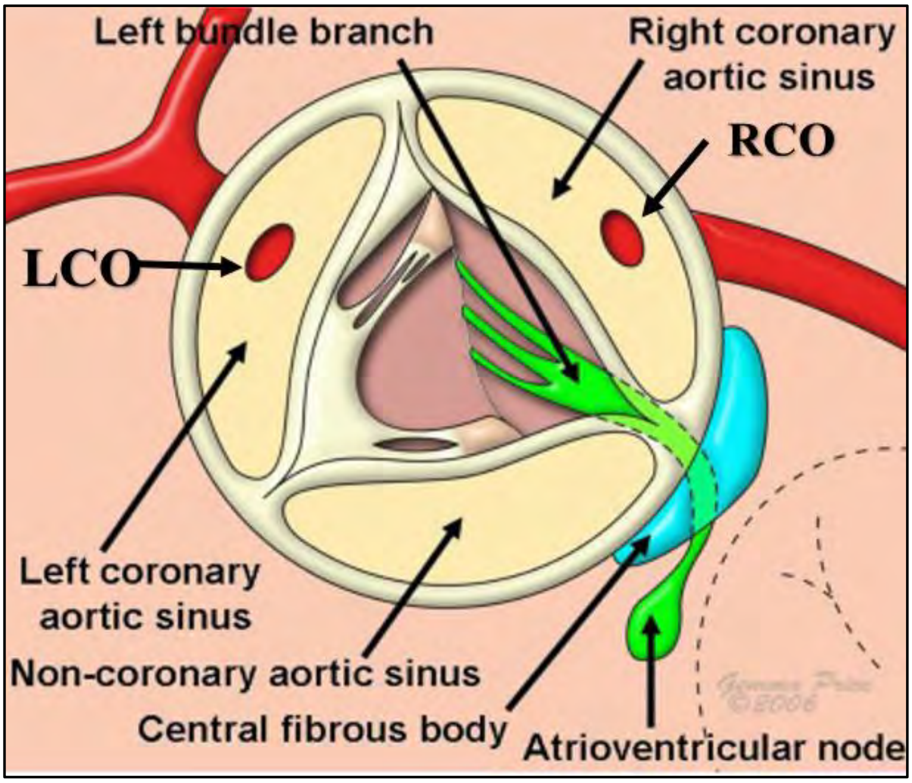

Figure 5*: A diagrammatic representation of the aortic valve from a superior view showing the relationship between the valve and atrioventricular node and bundle. (Adapted from Anderson, 2007)*

KEY*:* **LCO** = Left coronary ostium, **RCO** = Right coronary ostium

Histologically, the intimal, medial and external layers have different thicknesses from the level of the aortic annulus to the sino-tubular junction, suggesting that there are differences in biomechanics within the aortic root wall (Butcher *et al.*, 2002). The aortic root can be divided into four anatomical components viz. (i) the aortic annulus; (ii) leaflets (cusps); (iii) aortic sinuses (sinuses of Valsalva) and (iv) the sino-tubular junction (David, 1999) (Figure 6).

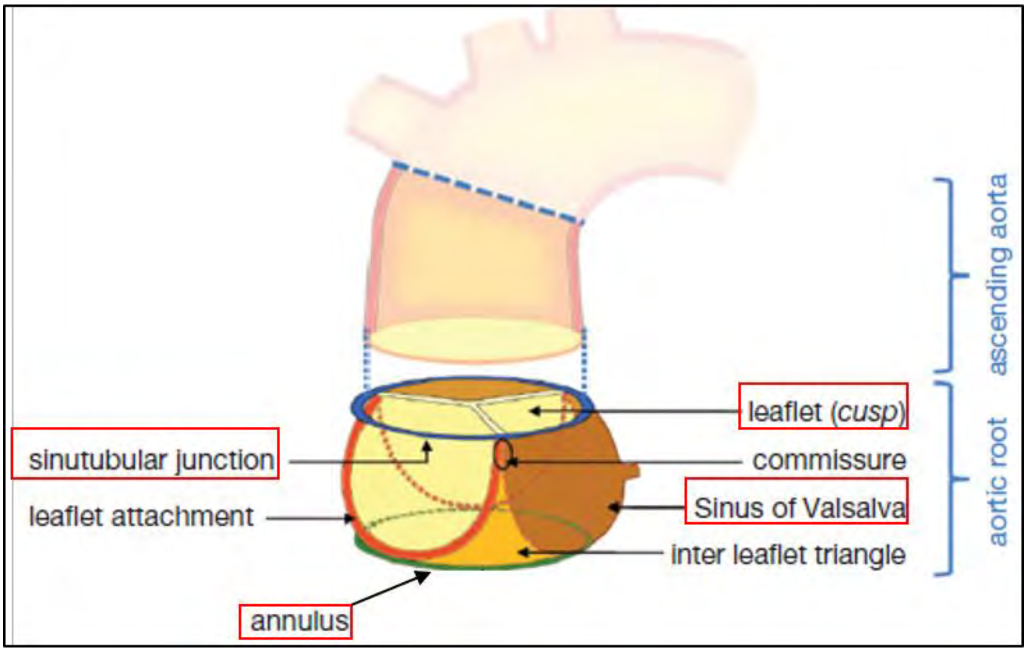

***Figure 6**: A diagrammatic representation of the aortic root showing the four components (i) annulus,(ii) leaflets,(iii) aortic sinuses and the (iv) sino-tubular junction (Adapted from Charitos and Sievers 2013).*

2.3.2 AORTIC ANNULUS

Controversy has characterised the definition and description of the aortic annulus for decades (Underwood *et al*., 1999; Anderson, 2009; Charitos and Sievers, 2012; Tilea *et al.,* 2013). The term 'annulus' refers to a ring or circle (Underwood *et al*., 1999). However, no anatomically or histologically circular or ring-like structure exists (Anderson, 2000). The annulus has been previously described as the ventriculo-aortic junction but this definition has been disputed since the 'anatomical ventriculo-arterial junction' represents the point where the left ventricular myocardium meets the aorta and there is a ring structure present at this position (Charitos and Sievers, 2012) (Figure 7).

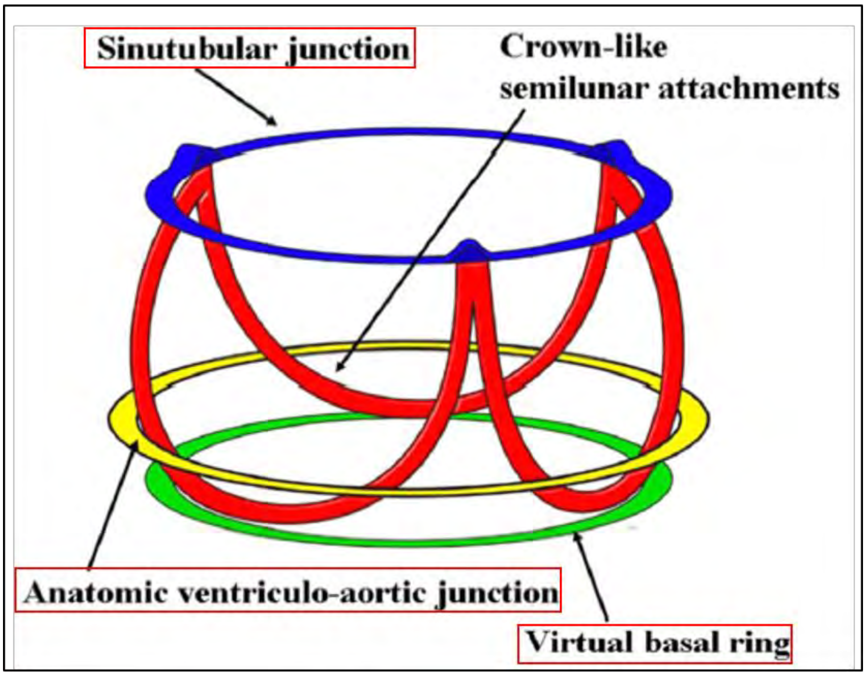

Figure 7*: The diagrammatic representation of the skeleton of the aortic valve showing three rings viz. virtual basal ring (the most proximal), anatomic ventriculo-aortic junction and sino-tubular junction and their relationship with the attachments of the cusps. (Adapted from Piazza et al., 2008)*

The term 'annulus' is popular because it describes the narrowest portion of the aortic root. (Charitos and Sievers, 2013). Conventionally, the annulus is the virtual or imaginary ring formed by the lowermost attachments of the aortic valve leaflets (Tilea *et al.,* 2012; Charitos and Sievers, 2013) (Figures 7 and 8). The annulus is continuous with the fibrous skeleton of the heart which forms three fibrous attachments for the semi lunar attachments of the cusps (Standring *et al.,* 2008). The annulus is located proximal to the ventriculo-arterial junction (Anderson, 2007).

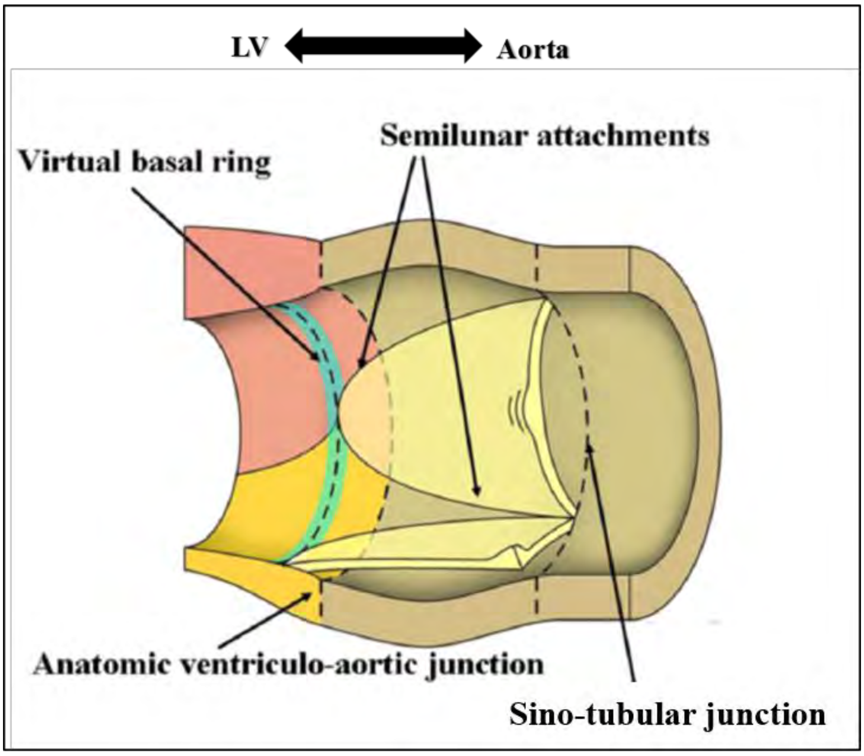

Figure 8*: A coronal view of the aortic root, showing the virtual basal ring (aortic annulus) at the most inferior attachment of the valve leaflets (Adapted from Anderson, 2007).*

Key**: LV** = Left ventricle

2.3.3 AORTIC VALVE LEAFLETS

Leonardo da Vinci drew sketches of aortic valves with 2, 3, and 4 cusps and he concluded that a valve with 3 leaflets had the optimal relation between anatomy and function (Mills *et al.*, 1978) .The normal aortic valve has 3 leaflets (tricuspid) in nature, however some individuals have 2 leaflets (bicuspid) and 4 leaflets (quadricuspid) (Standring *et al.*, 2008) (Figure 9). In clinical terms, the leaflets are labelled according to their relationship to the openings of the coronary artery viz. right, left and non-coronary leaflets (Standring *et al.*, 2008) (Figure 9). Anatomically, the right, left and non-coronary leaflets are known as anterior, left posterior and right posterior, respectively (Standring *et al.*, 2008). In the fetus, the right, left and non-coronary leaflets are also known as the posterior, right and left leaflets, respectively (Standring *et al*., 2008).

In a normal tricuspid aortic valve, the leaflets are attached within the aortic root following a scalloping or 'crown-like' pattern extending to the sino-tubular junction of the aorta (Anderson, 2000) (Figures 9). The scalloping pattern follows a fibrous structure which is part of the fibrous skeleton of the heart (Charitos and Sievers, 2013). The structure of a valve leaflet can be divided into three parts: (i) the free margin, with a thickened node (nodule of Arantius); (ii) the "belly" of the leaflet; (iii) the cusp attachments (Charitos and Sievers, 2013).

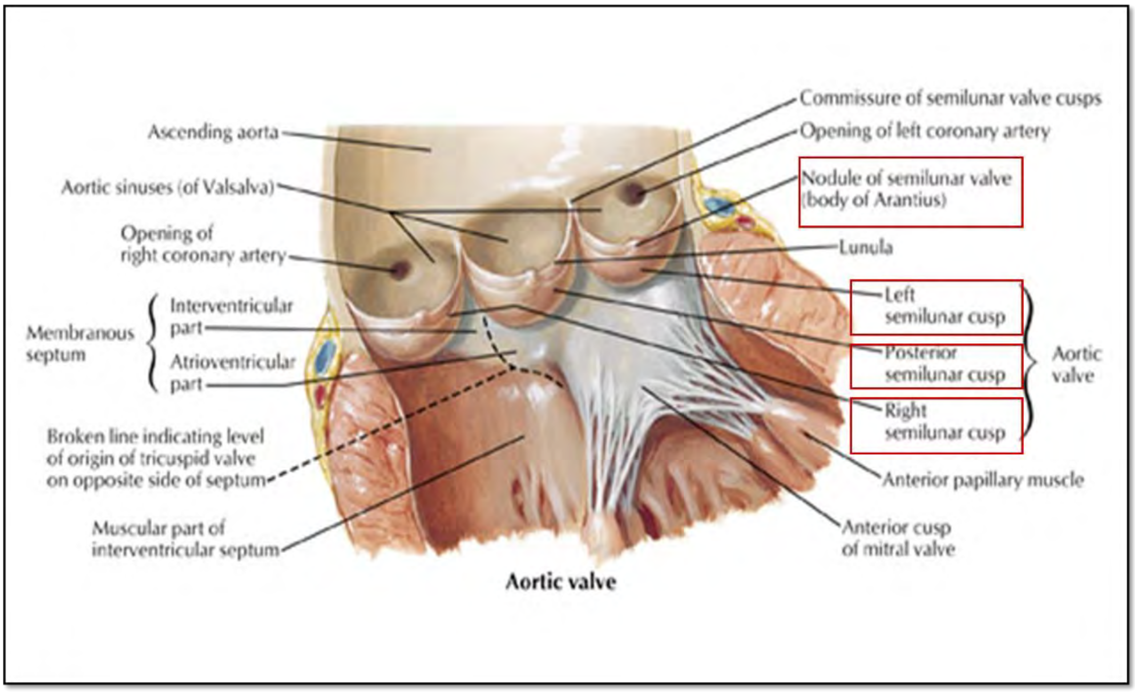

Figure 9*: The aortic root dissected open showing the 3 aortic valve cusps viz. left, posterior (non-coronary) and right cusps. The nodule of Arantius is also shown.*

(Adapted from Fiss, 2007)

The valve leaflets are thin, flexible structures which seal the lumen of the aortic root by coaptation during diastole (Butcher *et al.,* 2011). The histology of each valve shows three layers viz. the fibrosa, ventricularis and spongiosa (Christie, 1992). The fibrosa covers the aortic side of the leaflet and the ventricularis is thinner and is located on the ventricular surface of the leaflet whilst the gelatinous spongiosa lies in the middle (Vesely, 1998) (Figure 10).

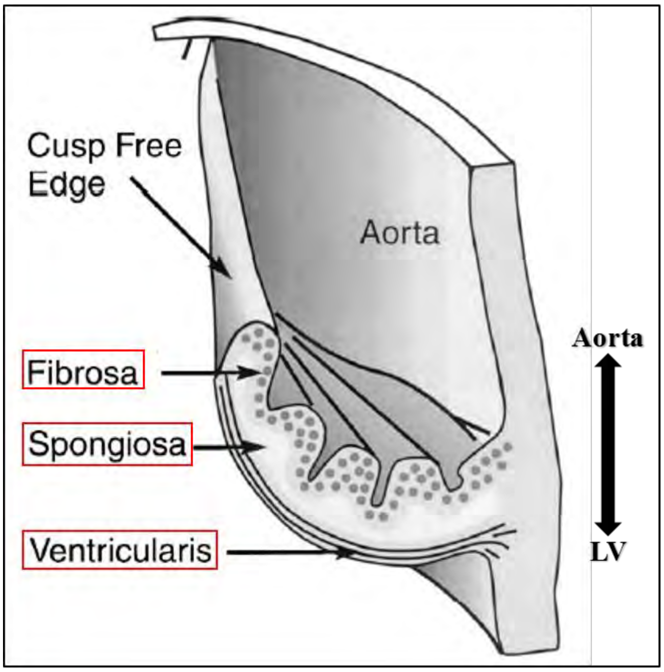

Figure 10*: Coronal section of the cusp and aortic wall showing the structure of the fibrosa, spongiosa and ventricularis (Adapted from Vesely, 1998).*

Key**: LV** = Left ventricle

The aortic valve leaflets form the hemodynamic junction between the left ventricle and the aorta (Anderson, 2000). All the structures proximal to the haemodynamic junction are subjected to ventricular pressures, whereas all the distal parts are subjected to aortic pressures (Charitos and Sievers, 2013). The leaflets meet at the co mmissures and the space between each leaflet is called the inter-leaflet triangle or trigone.

Bicuspid aortic valves (BAV) are composed of two leaflets, anatomically and functionally, however, most forms of a BAV have three embryological leaflets and co mmissures which later fuse to form two leaflets (Sievers and Schmidtke, 2007) (Figure 11). It has been labelled the co mmonest congenital cardiac anomaly in humans with a prevalence of 1-2% in the general population (Yerner *et al.*, 2002; Braverman *et al*, 2005, Sievers and Schmidtke, 2007).

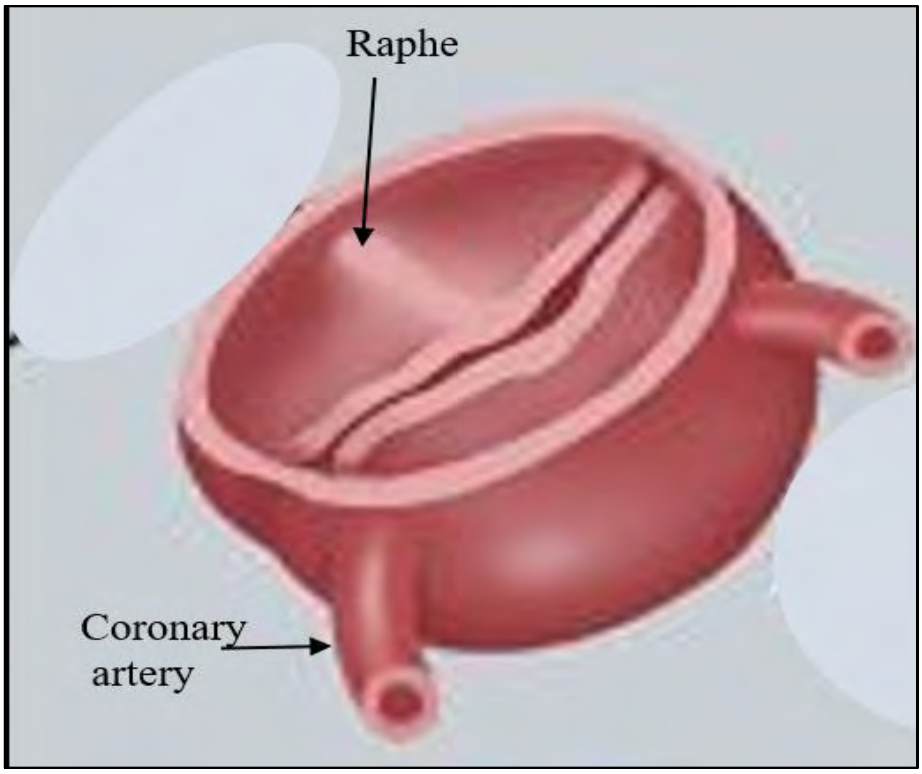

Figure 11*: A bicuspid aortic valve with two cusps, two co mmissures and a raphe (Adapted from Siu et al., 2010).*

There is a male predominance in the prevalence of BAV with ratios ranging from of 2:1 to 3:1 (Wachoupe, 1927; Yerner *et al.,* 2002; Siu *et al.,* 2010). BAV are usually characterised by two unequal cusps with a false co mmissure or raphe, which is the area of fusion in the larger cusp (Yerner *et al*., 2012).

According the Sievers and Schmidtke (2007), BAV can be classified into three main variances:

(i) Type 0: The "pure" form of BAV with two equal leaflets and no raphe (Figure 12a)

(ii) Type 1: Two unequal leaflets with one raphe (Figure 12b). This is the co mmonest type.

(iii) Type 2: The aortic valve with two raphae (Figure 12c).

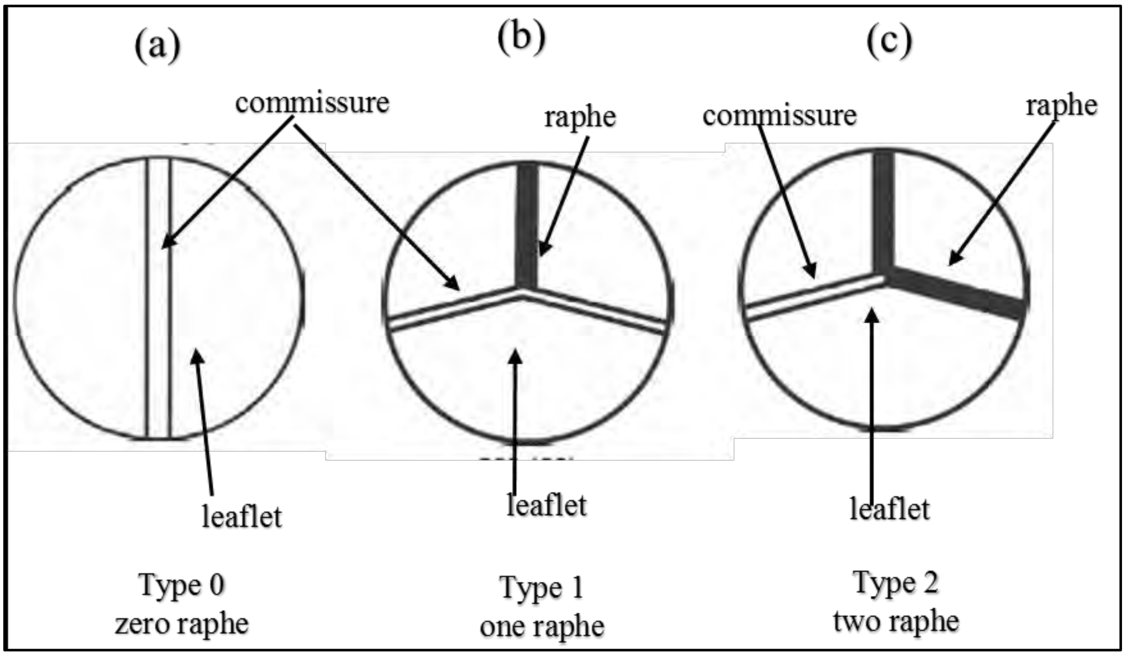

Figure 12*: An illustration showing three basic types of BAV showing leaflets, co mmissures and raphe (Adapted from Sievers and Schmidtke, 2007).*

The incidence of BAV is much higher in patients who present with aortic valve disease. In a series of 374 cases, BAV was noted to cause aortic stenosis in 46% of patients at the Mayo Clinic in the United States of America (Subramanian *et al*., 1984). A high number of patients, quoted as 49% to 61%, undergoing aortic valve replacement (AVR) present with BAV (Davies *et al.,* 1996; Robert and Ko, 2005). Unicuspid aortic valve (UAV) and Quadricuspid aortic valve (QAV) are more rare variations present in 0.02% and 0.0008% of the population, respectively (Novaro *et al.,* 2003 and Xiao *et al.*, 2010).

2.3.4 AORTIC SINUSES

Aortic sinuses are three dimensional spaces bounded by the aortic wall on the external surface and the leaflet on the internal surface. They are also bounded proximally by the attachments of the cusps and distally by the sino-tubular junction (Standring, 2008) (Figures 9 and 13).

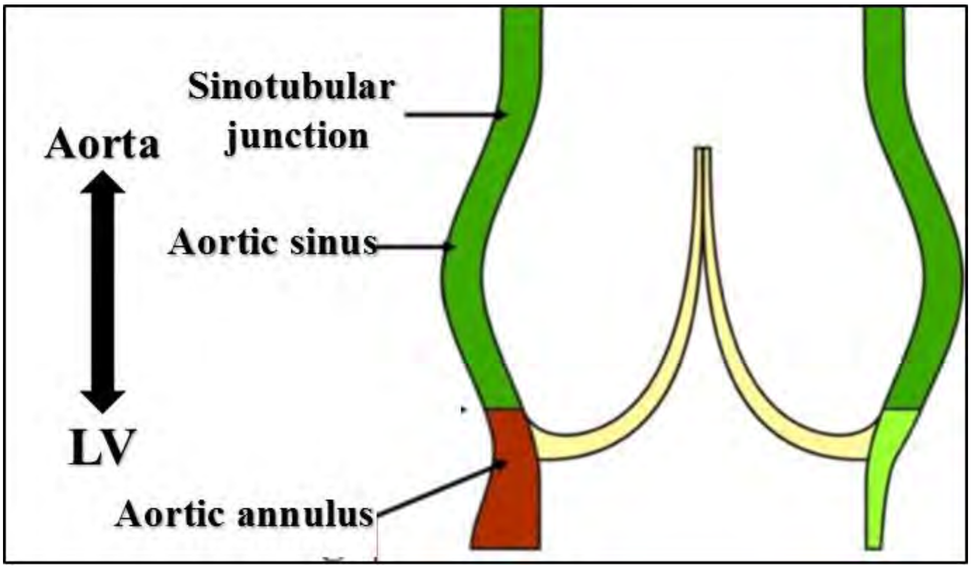

Figure 13*: Diagra mmatic representation of the dilation in the wall of aortic root viz. the aortic sinus (Anderson, 2007)*

***KEY*: LV** = Left ventricle

The sinuses were first described by Antonio Maria Valsava in 1740 (Reid, 1970). These are the areas into which the cusps open during systole (David, 1999). Two of them contain the coronary ostia, the opening for the coronary arteries, while one has no related coronary ostium viz. right and left aortic sinuses and a non-coronary sinus (Standring *et al.,* 2008). The non-coronary sinus is the largest of the three sinuses, followed by the right then the left (Choo *et al*., 1999 and Underwood *et al.,* 2000). During diastole, when backflow forces the apposition of the cusps, blood collects in these sinuses and is forced into the coronary arteries through their respective ostia (Butcher *et al*., 2002).

2.3.5 SINO-TUBULAR JUNCTION

The sino-tubular junction, also known as the supra-aortic ridge, is formed by the distal boundary of the aortic sinuses and thereby marks the beginning of the ascending aorta (Ho, 2009 and Sievers *et al*., 2012) (Figure 14).

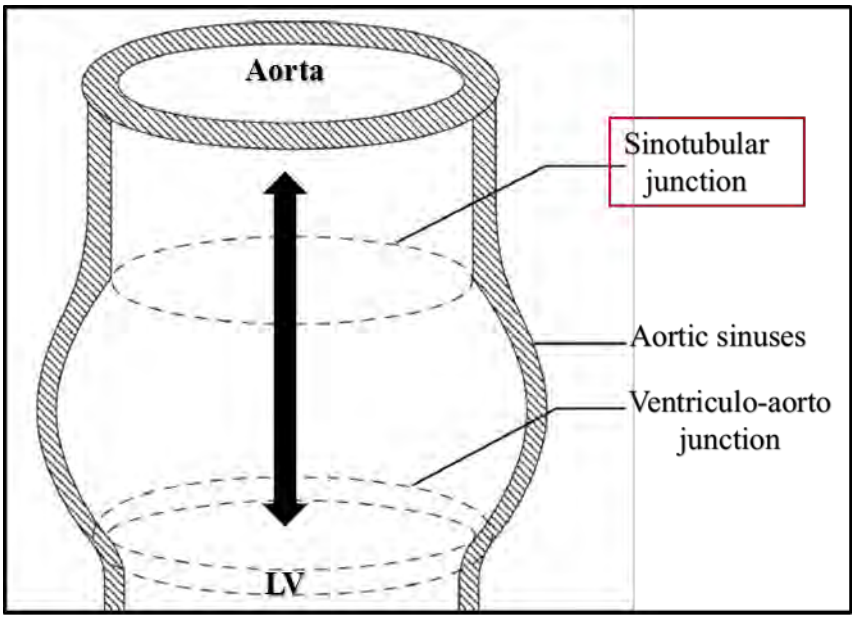

Figure 14*: An illustration of the aortic root showing the position of the sino-tubular junction (Adapted from de Kerchove and El Khoury, 2013)*

***KEY*: LV** = Left ventricle

The diameter of the aortic annulus has been described as 10 to 20% smaller than the diameter of the aorta at the sino-tubular junction (Kunzelman *et al.* (1994); Marom *et al*., 2013) and in the report by Zhu and Zhao in 2012, the annulus diameter averaged 70% of the sino-tubular junction. There is a gradual decrease in fibrous tissue and an increase in elastic material in the aortic wall from the annulus to the sino-tubular junction as the elastic fibres blend into the tunica media of the aortic wall (Ho, 2009).

2.3.6 CORONARY OSTIA

Cardiac muscle receives blood supply from the aorta through the left and right coronary arteries. Coronary arteries arise from the right and left aortic sinuses through the right and left coronary ostia, respectively (Standring *et al.,* 2008) (Figure 15).

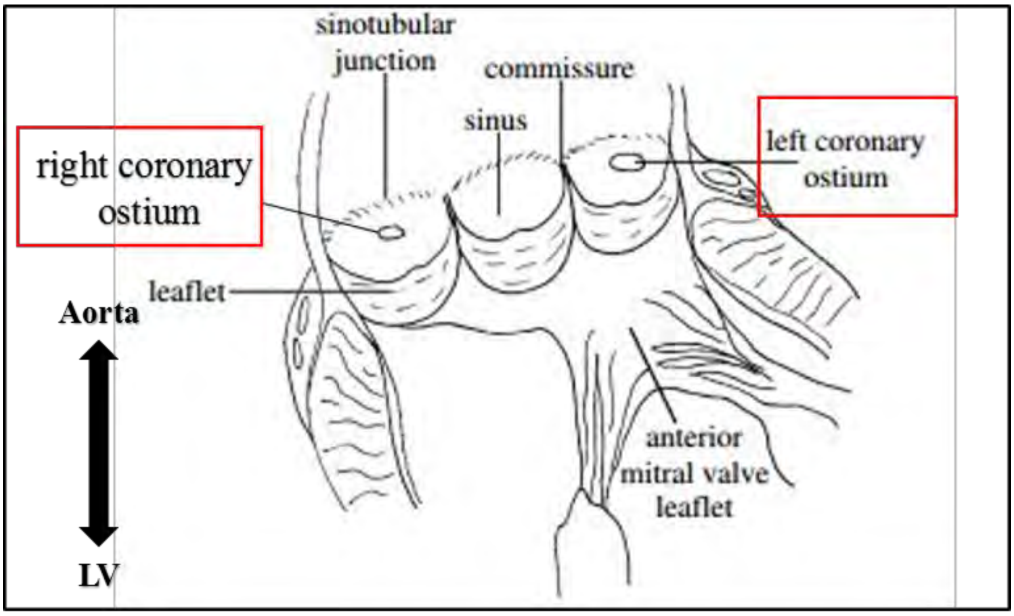

Figure 15: *A schematic diagram of a dissected aortic root showing right and left coronary ostia in the right and left aortic sinuses, respectively, both situated below the sino-tubular line (Adapted from Misfield and Sievers, 2007).*

(a) Shape of coronary ostia

Govsa *et al.* (2010), described three basic shapes of the coronary ostium viz. circular, ellipsoidal and crescentic. They reported that the most co mmon shape of left coronary ostium (LCO) was circular as noted in 52% of their cohorts, followed by ellipsoidal (35%) and lastly crescenteric at 13% (Govsa *et al*., 2010). Kulkarni and Paranjpe (2015) described the coronary ostia differently viz. circular, horizontally or vertically oval. For the right coronary ostium (RCO), they reported that the majority (76.6%) were horizontally oval, followed by 16% which were circular and 7% which were vertically oval (Kulkarni and Paranjpe, 2015). Furthermore, the frequency of LCO which were horizontally oval, circular and vertically oval was 73.3%, 23% and 10%, respectively (Kulkarni and Paranjpe, 2014). It is important to understand the various shapes of coronary ostia for clinical use since the use of catheterization in angiography and cardiac surgery requires well designed catheters that do not injure the coronary ostial wall (Di Mario and Sutaria, 2005).

(b) Position of coronary ostia

The RCO and LCO are typically found within the right and left aortic sinuses below the sino-tubular junction, respectively, although there are variations that have been described where the coronary ostia are found on or above the sino-tubular junction (Standring *et al*., 2008). According to Muriago *et al.* (1997), who dissected 23 normal hearts, the left and right coronary ostia were situated in aortic sinuses below the sino-tubular junction in 69% and 78% of cases, respectively. The frequency of the RCO located below the sino-tubular junction as reported in the literature was 60% (Calvacanti *et al*., 2003), 10% (Pejkovic *et al*., 2010), 78% (Govsa *et al*., 2010), 90% (Joshi *et al*., 2010), 83% (Kaur *et al*., 2012) and 62% (Sirikonda and Sreelatha, 2012) The frequency of RCO located on the sino-tubular junction was 12%

(Calvacanti *et al.,* 2003) and 71% (Pejkovic *et al*., 2008), 9% (Govsa *et al.,* 2010), 6% (Joshi *et al*., 2010), 14% (Kaur *et al*., 2012) and 11% (Sirikonda and Sreelatha, 2012). The frequency of RCO situated above the sino-tubular junction 28% (Calvacanti *et al.,* 2003), 19% (Pejkovic *et al*., 2008), 13% (Govsa *et al*., 2010), 6% (Joshi *et al*., 2010), 3% (Kaur *et al*., 2012) and 26% (Sirikonda and Sirikonda, 2012) (Table 2).

Table 2*: Comparison of location of right coronary ostia with respect to sino-tubular junction in different population groups.*

Author (year)	**Sample size (n)**	**Position in relation to SJ (%)**			**Country**
		Below	***At***	***Above***	
Calvacanti *et al.* (2003)	51	42	18	40	Brazil
Pejkovic *et al.* (2008)	150	18	22	60	Austria
Govsa *et al.* (2010)	100	58	13	29	Turkey
Joshi *et al* (2010)	105	80	15	5	India
Kuar *et al* (2011)	77	78	15	7	India
Sirikonda and Sreelatha (2012)	100	44	20	36	India
Weighted mean		**51**	**19**	**32**	

Key*:* **SJ** = Sino-tubular junction

The frequency of LCO located below the sino-tubular junction has been recorded as 42% (Calvacanti *et al.,* 2003), 18% (Pejkovic *et al.*, 2008), 58% (Govsa *et al*., 2010), 80% (Joshi *et al.,* 2010), 58% (Kaur *et al*., 2012) and 44% (Sirikonda and Sreelatha, 2012). The frequency of LCO located on the sino-tubular junction was 18% (Calvacanti *et al.,* 2003), 22% (Pejkovic *et al.,* 2008), 13% (Govsa *et al.,* 2010), 15% (Joshi *et al.,* 2010), 15% (Kaur *et al*., 2012) and 19% (Sirikonda and Sreelatha, 2012). The frequency of LCO situated above the sino-tubular junction was 40% (Calvacanti *et al*., 2003), 60% (Pejkovic *et al.,* 2008), 29% (Govsa *et al.,* 2010), 15% (Joshi *et al.,* 2010), 7% (Kaur *et al*., 2012) and 36% (Sirikonda and Sreelatha, 2012) (Table 3).

***Table 3**: Comparison of location of left coronary ostia with respect to sino-tubular junction in different population groups.*

Author (year)	**Sample size (n)**	**Position in relation to SJ (%)**			**Country**
		Below	***At***	***Above***	
Calvacanti *et al.* (2003)	51	42	18	40	Brazil
Pejkovic *et al.* (2008)	150	18	22	60	Austria
Govsa *et al.* (2010)	100	58	13	29	Turkey
Joshi *et al.* (2010)	105	80	15	5	India
Kaur *et al.* (2012)	77	78	15	7	India
Weighted mean		**48**	**17**	**31**	

The distance of the coronary ostia from the aortic annulus is often used to locate coronary orifices and this distance or height of the coronary ostium is measured from the bottom of the corresponding aortic sinus to the lower margin of the coronary ostium. The RCO is generally located higher than the LCO (Calvacanti *et al*. 2003; Joshi *et al*., 2010). The mean distance between the RCO and aortic annulus as reported in the literature was 13.2 mm (Calvacanti *et al*., 2003), 14.9 mm (Knight *et al*., 2009), 13.4 mm (Akhtar *et al*., 2009) and 14.1 mm (Joshi *et al*., 2007). The mean distance between the LCO and the aortic annulus according to the literature available was 12.6 mm (Calvacanti *et al*., 2003), 16.0 mm (Knight *et al*., 2003), 15.6 mm (Akhtar *et al*., 2009), 13.3 mm (Joshi *et al*., 2007) and 10.3 mm (Ribeiro *et al*., 2013) (Table 4). However, in pathological conditions such as aortic stenosis the distance between coronary orifices and aortic annulus maybe reduced significantly (Ribeiro *et al*., 2013).

***Table 4**: Comparison of the height of RCO and LCO from the aortic annulus.*

Author (year)	**Sample size (n)**	**Height of RCO from aortic annulus (mm)**	**Height of LCO from aortic annulus (mm)**
Calvacanti *et al* (2003)	51	13.2±2.64	12.6±2.61
Knight *et al* (2003)	75	14.9±4.3	16.0±3.6
Akhtar *et al* (2009)	25	15.2±2.5	15.6±2.7
Joshi *et al* (2010)	103	14.1	13.3
Ribeiro *et al* (2013)	24	No report	10.3±1.6
Weighted mean		**14.3**	**13.8**

Footnote: Calculation of weighted mean excludes Ribeiro et al., (2013) for height of RCO (no reported value). Consequently, the total sample number is: RCO = 254, LCO =278.

High take-off coronary ostia have attracted clinical attention due to their association with sudden death phenomena (Angelini, 2002 and Rosenthal *et al.*, 2012). They are typically located 1 cm superior to sino-tubular junction (Waller *et al.,* 1992). Motamedi *et al.* (2009) reported a case of a right coronary artery located 5 cm above the sino-tubular junction.

(c) Diameter of the coronary ostia

The LCO is usually larger than the RCO (Pejkovic *et al.,* 2008; Govsa *et al.*, 2010; Bhimali *et al.,* 2011) (Table 5). The LCO diameter ranges from 2.8 mm to 5.6 mm (Pejkovic *et al.,* 2008; Govsa *et al.,* 2010; Kaur *et al.*, 2012) the RCO diameter ranges from 1 mm to 4.5 mm. Of the literature reviewed, the mean diameter was 3.57 mm for RCO and 4.42 mm for LCO.

Table 5*: Comparison of the right and left coronary ostial diameters.*

Author (year)	**Sample size (n)**	**RCO diameter (mm)**	**LCO diameter (mm)**	**Country**
Calvacanti *et al.* (2003)	51	3.46±0.94	4.75±0.94	Brazil
Pejkovic *et al.* (2008)	150	3.6	4.1	Austria
Govsa *et al.* (2010)	100	3.32±0.82	4.22±0.72	Turkey
Kaur *et al.*(2012)	77	3.9±1.0	4.6±1.0	India
Weighted mean		**3.6**	**4.3**	

Key: **RCO** = right coronary ostium, **LCO** = left coronary ostium

In a series of 500 heart specimens, Sahni and Jit (1989) reported that the diameters of coronary arteries had a significant relationship with weight, body surface area (BSA), heart weight and age. The study showed that the size of the coronary arteries increased with an increase in age (Sahni and Jit, 1989). Ilayperuma and colleagues (2011), showed clearly that the calibre of coronary arteries was smaller in females than males. The same results were reported by Hiteshi *et al*. (2014), who did their studies in 4200 subjects but they also reported that there was no significant relationship between the diameter of coronary arteries and age, height, weight, body mass index and BSA.

2.4 EMBRYOLOGY OF THE AORTIC ROOT

During the third week of fetal life, the embryo develops a vascular system to distribute nutrients to the rest of the body after diffusion becomes insufficient to distribute nutrients (Tilea *et al*., 2012). Progenitor heart cells form the primary heart field, a horseshoe-shaped cluster of cells (Sadler, 2013) (Figure 16).

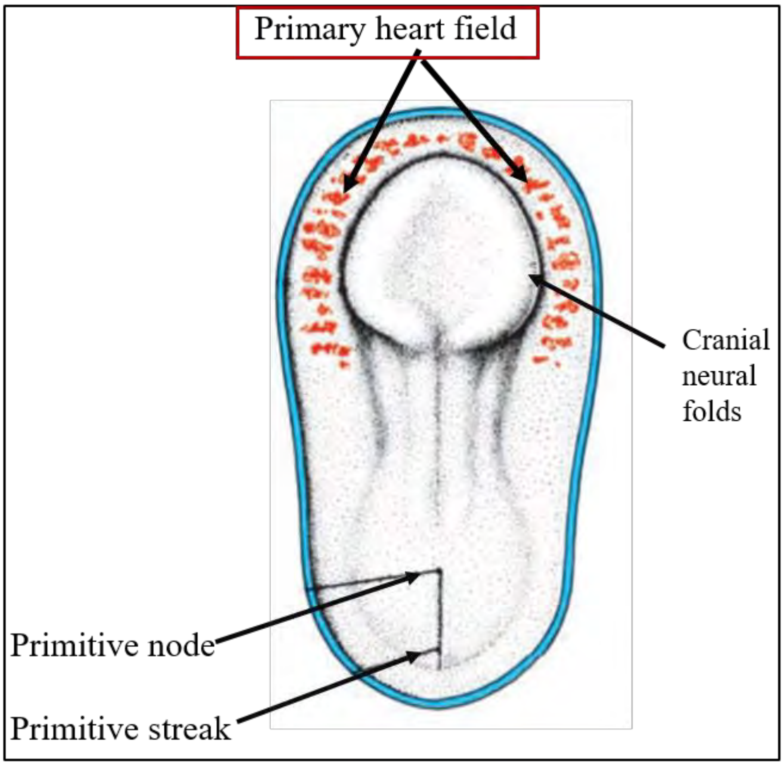

Figure 16*: Dorsal view of an 18 day old embryo showing the horse-shoe cluster of cells forming the primary heart field (Adapted from Sadler, 2013)*

The primary heart field will later give rise to the right and left atria, left ventricle and most of the right ventricle. The other part of the right ventricle and outflow tract is derived from the secondary heart field (Sadler, 2013) (Figure 17).

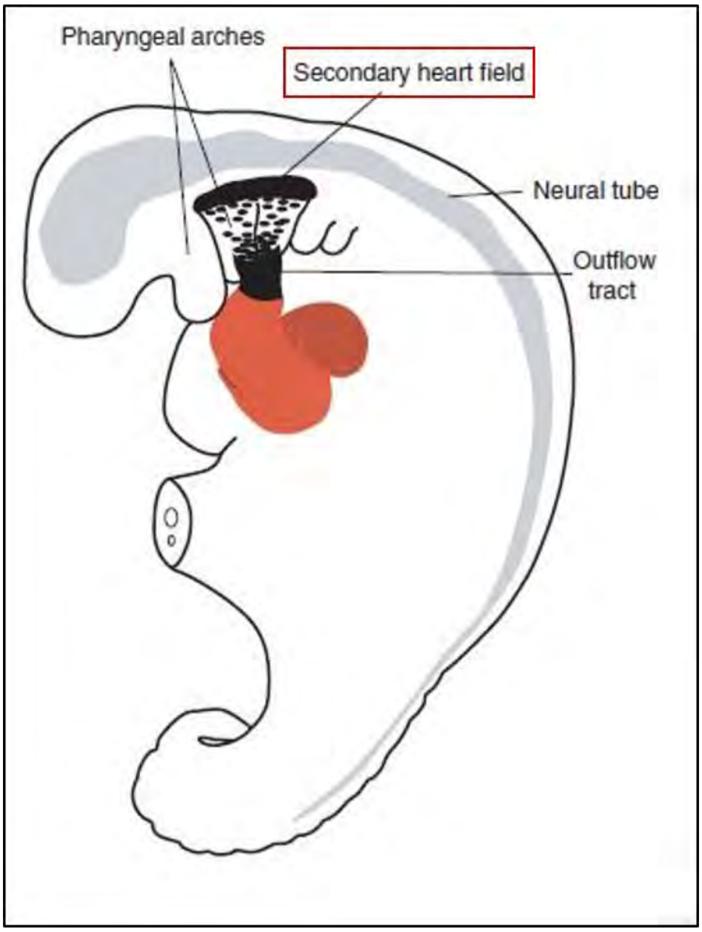

Figure 17*: The embryo shown in the coronal view showing the secondary heart field forming the outflow tract (Adapted from Sadler, 2013).*

These heart fields will fuse, bend and fold to give a heart tube which will have three layers viz. endocardium, myocardium and epicardium (Anderson *et al.,* 2002). The outflow tract, which is made up of the truncus arteriosus and conus cordis, develops a septum during the fifth week (Pires-Gomes and Perez-Pomares, 2013). As the outflow tract grows, the heart tube starts bending ventrally, caudally and to the right (Sadler, 2013) (Figure 18).

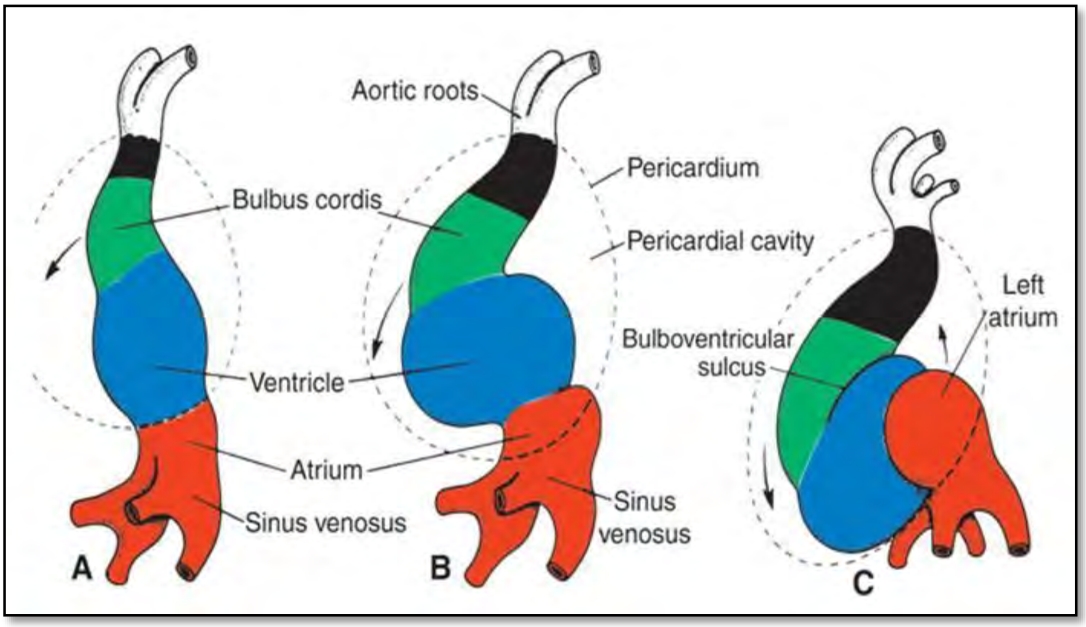

***Figure 18**: The outflow tract (truncus arteriosus and conus cordis) during cardiac loop bending on day 23 (Adapted from Sadler, 2013)*

This septum separates the truncus arteriosus into the aorta and pulmonary trunk, whilst the mesenchymal swellings are developing into cusps of the aortic and pulmonary valves (Figure 19).

The coronary arterial system becomes the main supply of nutrients to the heart during the fifth week of development (Sadler, 2013). Coronary arteries develop from the epicardial cells and angioblasts from the sinus venosus and they invade the aorta thereby establishing coronary ostia in the aortic root (Anderson *et al.,* 2002). At the end of the eighth week of development, the foetus has a fully functioning heart (Tilea *et al.,* 2012).

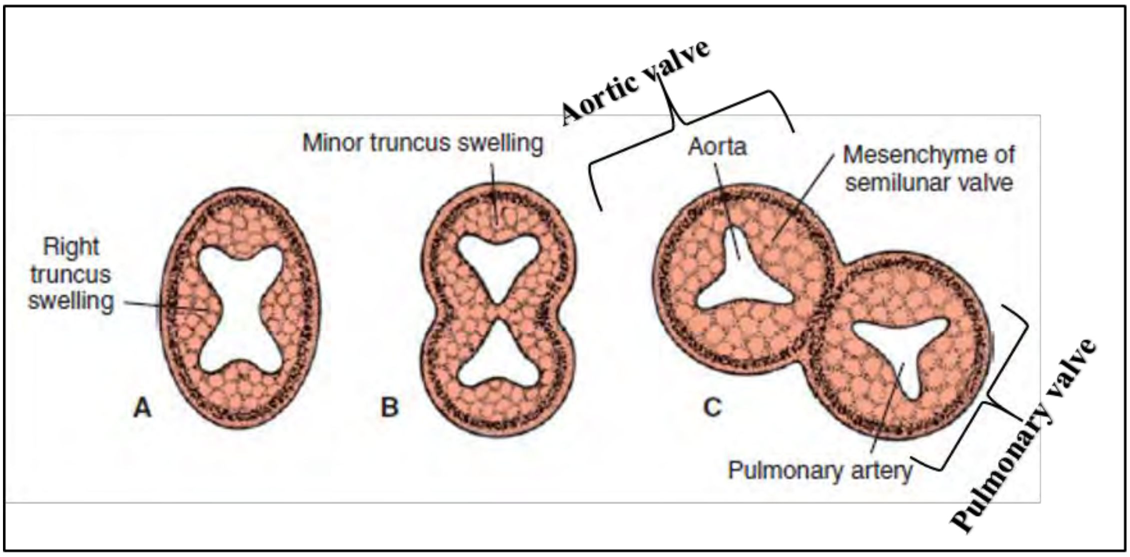

Figure 19: *Transverse sections through the truncus arteriosus at the level of the semilunar valves at week 5 (Adapted from Sadler, 2013).*

2.5 FUNCTIONS OF THE AORTIC ROOT

The aortic root is the whole functional unit of the aortic valve and the relationship between each component is important for valve opening and closure (Anderson, 2007). The aortic root is the pathway for oxygenated blood to the rest of the body and to understand the role of the aortic valve, it is important to understand that the cardiac cycle consists of two phases viz. systole and diastole (Nishimura, 2002). During systole, cardiac muscle contracts, pressure in the left ventricle increases exponentially, the aortic valve opens and blood is squeezed out of the left ventricle into the aorta (Figure 20).

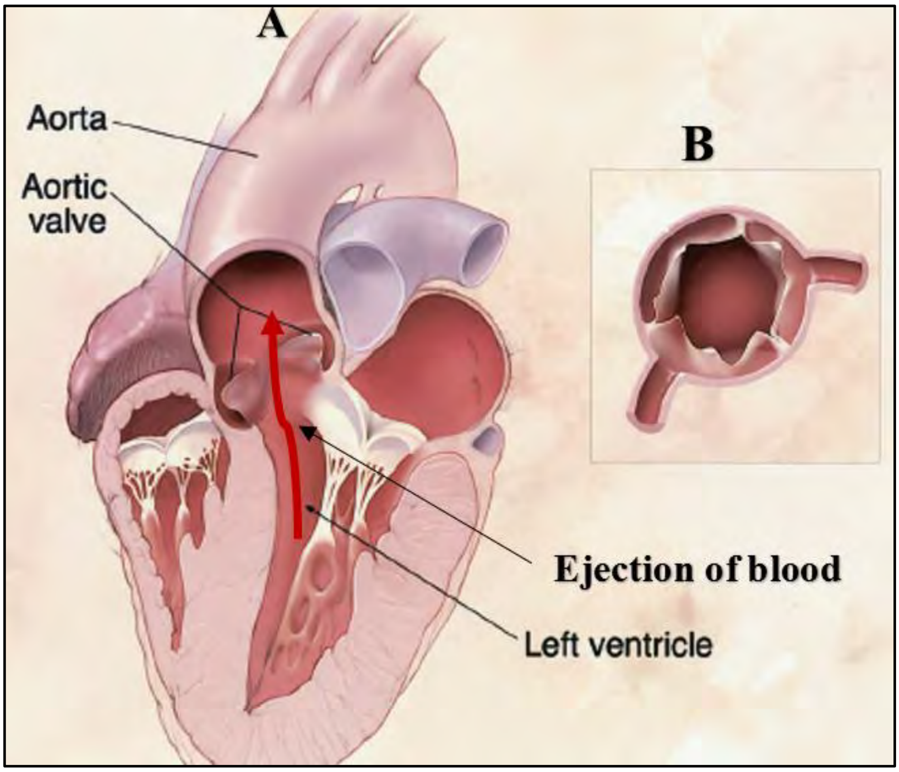

***Figure 20**: A diagra mmatic representation of the heart in systole. A: Arrow shows the movement of blood from the left ventricle into the aorta through an open aortic valve. B: Superior view of an open aortic valve (Adapted from Nishimura, 2002)*

Since the annulus is part of the fibrous skeleton of the heart, it is relatively resistant to distention and the diameter of the annulus rarely changes during these two phases (Standring *et al.*, 2008). The relative non-pliability of the aortic annulus and the jhhigh pressure generated during ventricular contraction allows blood to be ejected at maximum velocity, pushing the three cusps to open the aortic valve and allowing blood to be emptied into the aorta. However, at the level of the sino-tubular junction there are more elastic fibers than fibrous tissue in the aortic root wall and this allows the diameter of the aortic root to increase by 16 percent (Standring *et al.*, 2008).

During diastole, cardiac muscle relaxes and blood regurgitates back from the aorta forcing the coaptation of the semi-lunar valves and closure of the aortic valve (Figure 21). Blood fills in the aortic sinuses and this action pushes blood into the coronary arteries though their respective coronary ostia. Normal aortic sinuses promote a smooth, non-turbulent blood flow into the coronary vessels (Standring *et al*., 2008).

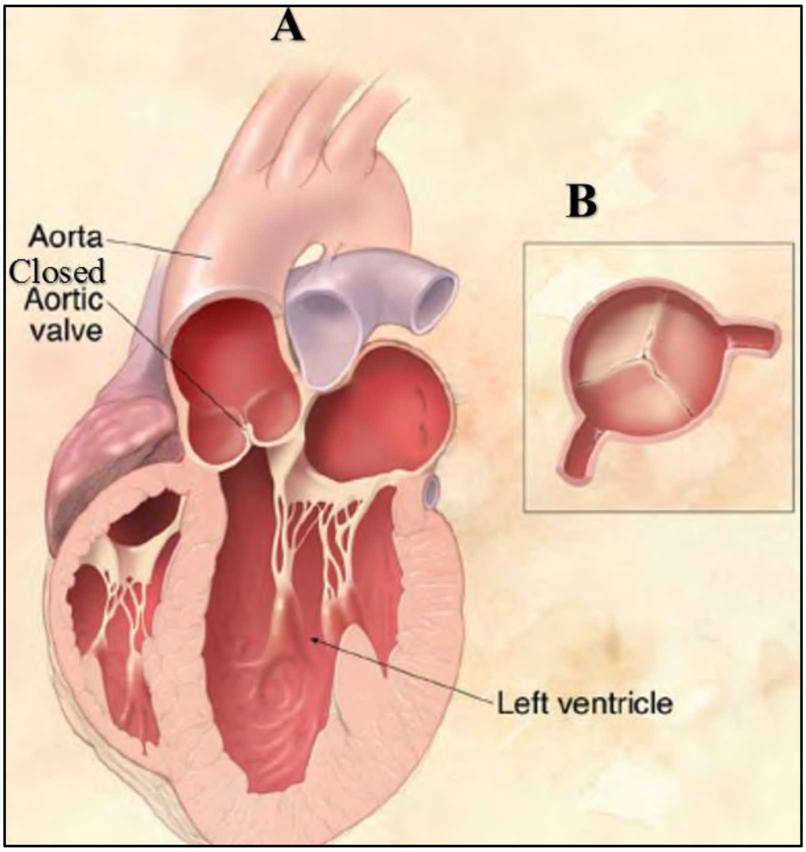

Figure 21*: A diagra mmatic representation of the heart in diastole. A: Closed aortic valve and a relaxed ventricle. B: Superior view of a closed aortic valve (Adapted from Nishimura, 2002)*

2.6 AORTIC VALVE REPLACEMENT (AVR) SURGERY

2.6.1 HISTORICAL BACKGROUND

AVR is a surgical operation where poorly functioning cusps are removed and replaced by an artificial valve to improve function and therefore relieve patients of their aortic valve disease symptoms (Townsend *et al.*, 2004). The first operation on a human heart recorded was done in 1896 by a German physician who sutured a knife wound (Baldwin *et al.*, 1994). Aortic valve stenosis was initially treated by passing dilators through the aortic root (Townsend *et al.*, 2004). The invention of the cardio-pulmonary bypass machine in the 1952 greatly advanced the field of cardiac surgery (Stoney *et al.,* 2009). In 1960, the first aortic valve transplant was performed using a mechanical valve (Baldwin *et al.*, 1994). Since then, there has been great improvement in the quality of prostheses and surgical techniques.

Over 200 000 patients with aortic regurgitation and stenosis undergo AVR each year worldwide (Brown *et al.*, 2009). Patients with aortic stenosis and regurgitation get their symptoms relieved by this procedure (Townsend *et al.*, 2004). Maximum relief of the symptoms depend on the size of the valve implanted after diseased cusps are removed (Townsend *et al.*, 2004). A good prosthesis has an orifice that allows adequate blood that meets the requirements of the body to be ejected. In practice, an ideal prosthesis may not fit in the aortic root because of the small dimensions and calcification narrows the aortic root and restricts elasticity of the aortic wall that may be associated with the individual and valve disease (Nick *et al.*, 1970; Borracci *et al.,* 2014).

2.6.2 NORMAL AORTIC ROOT DIMENSIONS

Normal aortic root diameters, cited in the available literature, have been measured in normal live patients using radiographic studies especially echocardiography (Vasan *et al.*, 1995; Evangelista *et al*., 2010; Zhu and Zhao, 2011; Son *et al*., 2013). The principal dimensions are usually measured at the level of the aortic annulus, aortic sinuses and sino-tubular junction (Biaggi *et al.*, 2009; Son *et al.*, 2013). The mean aortic annulus has been reported to have varying diameters viz. 20 mm (Tamas and Nylander, 2010), 20.4 mm (Zhi and Zhao *et al*., 2011), 23.3 mm (Son *et al*., 2013), 18.7 mm (Vriz *et al*., 2013) and 20.6 mm (Davies *et al*., 2014). The mean diameter at the aortic sinus level may range from 29 mm to 45 mm (Evangelista *et al*., 2010), 28.2 mm (Zhi and Zhao *et al*., 2011), 32.4 mm (Son *et al*., 2013), 28.5 mm (Vriz *et al*., 2013), 27.5 mm (Davies *et al*., 2014). The mean diameter at the sino-tubular junction ranges around 27 mm (Tamas and Nylander, 2007), 23.5 mm (Zhi and Zhao *et al*., 2011) and 26.1 mm (Son *et al*., 2013). The mean diameter at the sino-tubular junction may range around 26.9 mm and 24.4 mm (Vriz *et al*., 2013), and 24.4 and 21.6 mm in males and females respectively (Davies *et al*., 2014) (Table 6).

Table 6*: Su mmary of aortic root diameters as cited by different authors.*

Author (year)	**Sex**	**Sample size (n=)**	**Mean aortic root diameter(mm)**		
			Aortic annulus	**Aortic sinus**	**Sino-tubular junction**
Tamas and Nylander (2007)	Both	32	21	32	27
Biaggi *et al*. (2009)	Male	815	32	34	No report
	Female	984	30	31	No report
Zhi and Zhao *et al*. (2011)	Both	341	20.4	28.2	23.5
Son *et al*. (2013)	Both	112	23.3	32.4	26.1
Vriz *et al*. (2013)	Male	282	21	31.8	26.9
	Female	142	18.7	28.5	24.4
Davies *et al*. (2014)	Male	208	23.9	31.9	24.4
	Female	239	20.6	27.5	21.6
Weighted mean				**20.7**	**24.4**

Normal aortic root diameters vary among individuals but age, sex, weight, height and body surface area (BSA) are principal determinants of the size of the aortic root (Vasan *et al*., 1995; Tamas and Nylander, 2007; Devereux *et al*., 2012). The diameters of the aortic root tend to increase significantly with age from childhood (Biaggi *et al*., 2009; Vritz *et al*., 2011;

Zhu and Zhao, 2011; Wang *et al*., 2012; Son *et al*., 2013). Generally, males have wider aortic roots than females for the same age groups (Vasan *et al*., 1995; Tamas and Nylander, 2007; Devereux *et al*., 2012; Wang *et al*., 2012; Vritz *et al*., 2013). However, a report by Zhu and Zhao (2011), showed that while age, weight and height were principal determinants of aortic root sizes, there was no significant difference in size of the aortic root between males and females. Body surface area (BSA), calculated from height and weight of an individual, is more representative of the aortic valve area hence its clinical use to determine prosthetic sizes in AVR (Townsend *et al*., 2004; Biaggi *et al*., 2009; Zhu and Zhao *et al*., 2011; Wang *et al*., 2012; Devereux *et al*., 2012). Other determinants of aortic root size include mean arterial blood pressure (Vasan *et al*, 1995; Wang *et al*., 2012; Vritz *et al*., 2013) and heredity (Bella *et al*., 2012).

2.6.3 THE NARROW AORTIC ROOT

A narrow aortic root is usually defined in clinical terms as a root that accepts a prosthesis whose size has an effective valve area smaller than that of patient's normal native valve (Verrier *et al*., 2003). The important point to note, is the adequacy of the aortic annulus to accept a valve replacement device that would allow adequate blood to be ejected during systole (Franco and Verrier, 2003). The narrow aortic roots are frequently associated with size 19 mm and 21 mm prosthesis (Kulik *et al*., 2008). Aortic valve disease is frequently associated with an aortic annulus of smaller than normal size and this is especially likely when calcific aortic stenosis complicates pre-existing congenital aortic stenosis (Nicks *et al.*, 1970). Narrow aortic roots are more co mmon in women of small stature and have been found in 7 to 14% of patients undergoing AVR (Verrier *et al*., 2003; Borracci *et al.*, 2014).

For AVR surgery, the size of the prosthesis to be implanted can be determined by pre-operation echocardiographic measuring of the aortic root (Vasan *et al*., 1995), BSA and patient prosthesis mismatch (PM) prediction (Pibarot *et al*., 2009) as well as intra-operation sizing by the surgeon (Joshi *et al*., 2007). Small prosthetic valves can be obstructive, causing high pressure gradients between the left ventricle and aorta producing PPM (David, 1999). PPM was described by Rahimtoola in 1978 as "present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve". PPM means that the prosthetic valve does not allow ejection of blood at the same rate as a natural native valve during systole (Rahimtoola, 1978). Pibarot *et al.* (2009) defined PPM using the ratio of the orifice area of a prosthesis to the BSA, which became to be known as the effective valve orifice area index (EOAI). Using that ratio, PPM at an EOAI of above 0.85 cm^2/m^2 is clinically insignificant, below 0.85 cm^2/m^2 is moderately significant and below 65 cm^2/m^2 is severely significant (Table 7) (Pibarot *et al.,* 2009).

Table 7*: Values used of prosthetic valve EOAI for the identification and uantification of prosthesis-patient mismatch (PPM) (Adapted from Pibarot et al., 2009)*

Grade of PPM	Mild or Not Clinically Significant (cm^2/m^2)	Moderate (cm^2/m^2)	Severe (cm^2/m^2)
Index value	>0.85 (0.8-0.9)	≤0.85 (0.8-0.9)	≤0.65 (0.6-0.7)

An acceptable prosthetic size may be calculated from a PPM calculator using an individual's BSA (Table 8) (Carpentier-Edwards, 2007). The PPM calculator is a clinical tool designed to make it easier for surgeons to use a prosthesis which gives minimum PPM.

PPM has been associated with residual left ventricular outflow tract obstruction (Losenno *et al*., 2013), incomplete left ventricular mass regression (Tasca *et al.,* 2005), minimal or absent symptom relief (Losenno *et al*., 2013), increased early mortality (Blais *et al*., 2001) and late mortality (Kohsaka *et al.,* 2008). In order to reduce the occurrence of PPM, the largest possible prosthesis should be implanted (Castro *et al*., 2002).

***Table 8**: Prosthesis-Patient Mismatch (PPM) Calculator for porcine stented mechanical valves. This is used to calculate a good prosthesis using BSA which prevents PPM. (Adapted from Carpentier-Edwards, 2007)*

		EOAI by Valve Size (mm)			
	Valve size	**19**	**21**	**23**	**25**
	EOA1(cm²)	1.28	1.69	1.87	1.89
BSA (m^2)	**1.0**	1.28	1.69	1.87	1.89
	1.1	1.16	1.54	1.70	1.72
	1.2	1.07	1.41	1.56	1.58
	1.3	0.98	1.30	1.44	1.45
	1.4	0.91	1.21	1.34	1.35
	1.5	0.85	1.13	1.25	1.26
	1.6	0.80	1.06	1.17	1.18
	1.7	0.75	0.99	1.10	1.11
	1.8	0.71	0.94	1.04	1.05
	1.9	0.67	0.89	0.98	0.99
	2.0	0.64	0.85	0.94	0.95
	2.1	0.61	0.80	0.89	0.90
	2.2	0.58	0.77	0.85	0.86
	2.3	0.56	0.73	0.81	0.82
	2.4	0.53	0.70	0.78	0.79
	2.5	0.51	0.68	0.75	0.76

Key: **BSA** = Body surface area; **EOAI** = Effective orifice area index

Cardio-thoracic surgeons have developed various techniques to be able to insert a large size valve in patients with narrow aortic roots in order to overcome PPM.

i) Mechanical dilatation with a Hegar's dilator

Large valves have been successfully implanted in narrow aortic roots after dilatation with Hegar's dilators (Bartels and Sievers, 1999; Hata *et al.*, 2006).

ii) Oblique placement of the prosthesis

This technique allows a large prosthesis placement without surgically enlarging the aortic root. The prosthesis is placed obliquely and partially above the annulus taking advantage of the bulging coronary sinus (Ishida *et al.*, 2001). Supra-annular valve insertion still involves possible complications such as peri-valvular leakage, coronary ostia obstruction, and rupture of the noncoronary sinus (Ishida *et al.*, 2001).

iii) Shoe horning technique

When faced with a narrow aortic root, the surgeon may elect not to enlarge the aortic root but forcibly place or "shoe horn" a large prosthesis to sit on the aortic annulus. The procedure allows an otherwise large valve that would not fit to be implanted. There is paucity in the literature concerning its efficacy and safety since results have not been formally presented.

iv) Aortic root enlargement (ARE) techniques

Due to the problems associated with PPM in narrow aortic roots, Nick and colleagues (1970) developed a surgical method to enlarge the annulus diameter to allow implantation of a large prosthesis. The operation involves making an incision in the posterior aspect of the aortic root through the co mmissure between the left and non-coronary cusps extending to the origin of the mitral valve (Nicks *et al.*, 1970). A teardrop shaped patch is sutured in the space created to increase the diameter of the aortic root which allows insertion of a bigger size prosthesis (Nick *et al.,* 1970). This enlargement allows the surgeon to place a valve two sizes bigger than would usually fit.

Manougian and Seybold-Epting (1979) slightly modified Nick's procedure, by making the incision in the middle of the non-coronary sinus. A large patch is placed to close the defect and this increases the diameter by an average of 3 to 5 mm (Losseno *et al.,* 2013). The surgical methods developed by Nick *et al.* (1970) and Manougian *et al.* (1979) procedures are routinely performed in North America (Castro *et al.,* 2002).

Other procedures, such as aorto-ventriculoplasty are rarely performed as they are radical and reserved for patients with associated major cardiac abnormalities. This procedure utilises the individual pulmonary valve as the replacement for the diseased aortic valve and a cadaveric pulmonary aortic valve is used to replace the donor valve (Brown *et al.,* 2006). Aortic root enlargemant procedures are associated with an increased operation time, increased exposure of myocardium to hypoxic conditions and increased blood loss (Castro *et al.*, 2002).

2.6.4 CORONARY ARTERY STENOSIS AFTER AORTIC VALVE REPLACEMENT

Coronary artery stenosis with associated reduction of blood flow to the myocardium is a life-threatening complication of AVR estimated to be found in up to 5% of cases (Zaikas *et al.,* 2010). It has been noted to occur during and i mmediately after the operation usually 1 to 6 months post operation (Pillai *et al.,* 2004; Umran *et al.,* 2012). Coronary artery stenosis occurs in 1% of TAVI patients. In TAVI cases, it has been noted to occur with associated reduction of coronary ostial height as the ostium is displaced caudally (Ribeiro *et al.,* 2013).

(a) Early coronary stenosis

Coronary occlusion can occur when a prosthesis is implanted above the annulus and sutures are placed along the scalloping line of attachments for the native valve cusps (Choi *et al*., 2010; Ueda, 2010; Orihashi, 2013). Supra-annular placement of the prosthetic valve is often employed as a method to implant a larger valve without stretching or surgically enlarging the aortic valve (Tabata *et al.*, 2014). Placing sutures in a scalloped pattern up to the co mmissures deforms and potentially obstructs the ostia (Ueda, 2015) (Figure 22).

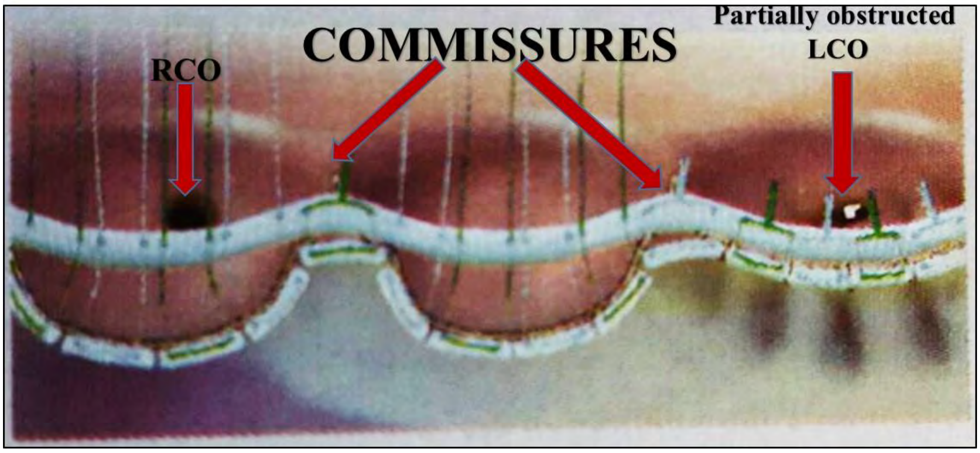

Figure 22*: A diagra mmatic illustration showing partial obliteration of the LCO when a valve is sutured high up starting from the co mmissures (Adapted from Ueda, 2010).*

KEY: **RCO** = right coronary ostium, **LCO** =left coronary ostium

When a large valve is implanted in a narrow aortic root, the valve can tilt upward occluding a coronary ostium (Tullirazi *et al.,* 2011). Pillai *et al*. (2004) reported anecdotes of coronary blood flow blockage as an acute complication of AVR caused by calcium debris embolization, occlusion by the prosthesis or oedematous reaction and ostial thrombosis due to trauma. Coronary artery spasm has also been reported to cause acute coronary blood flow blockage in patients undergoing AVR (Kinoshita *et al.,* 1991; Pragliola *et al.,* 2007).

Distortion in the structure with potential obstruction of the coronary ostia has also been observed in patients who had their prosthesis sutured following the scalloping pattern of the cusps (Choi *et al*., 2010) (Figure 23A).

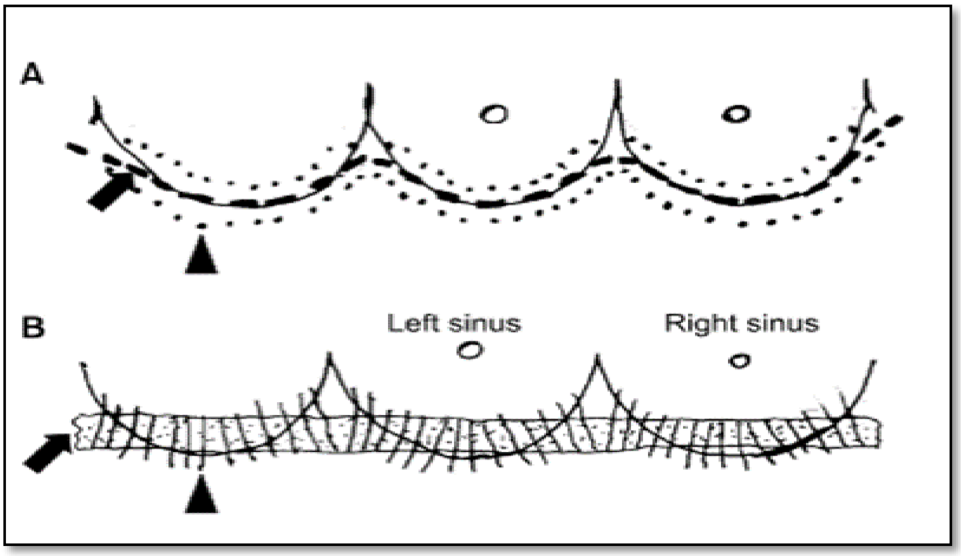

Figure 23: *(*A) *The stitches are placed in a wave-like fashion following the scalloping nature of the valve cusp attachment. (B) With the continuous suture technique, the prosthetic ring (arrow) is seated in the curvilinear suture line (arrowhead) (Adapted from Choi et al., 2010).*

Ueda (2010) and Choi *et al*. (2013) reco mmended suturing the prosthesis from the lowest point of the aortic annulus first, following the lowermost attachments of the valve cusps thereby creating a 'straight' suture line that does not follow the scalloped pattern (Figures 23B and 24). Avoiding the scalloped pattern reduces the chances of distorting and occluding the ostia (Ueda, 2010).

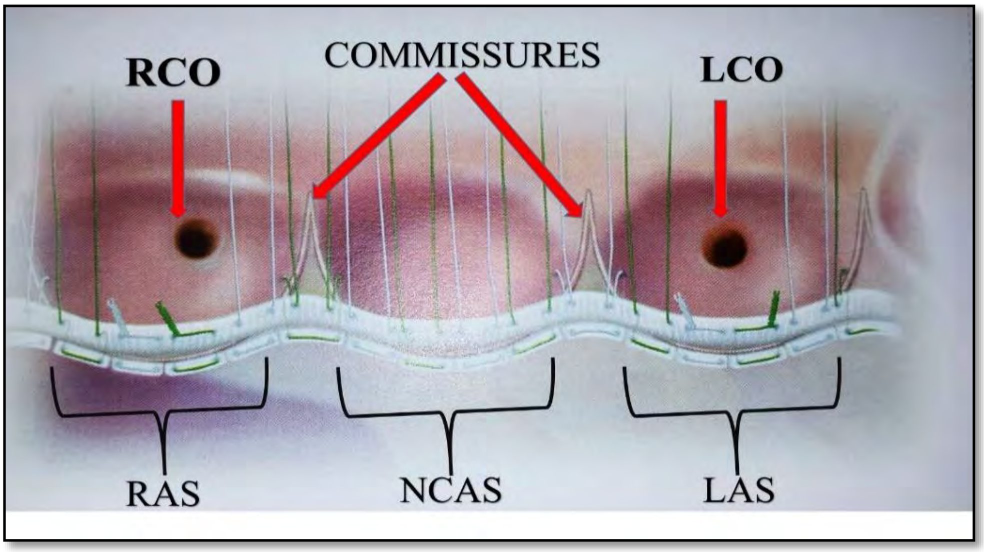

***Figure 24**: The reco mmended technique showing the valve sutured at the lowermost portion of the aortic annulus (Adapted from Uechi, 2010)*

Key: **RCO** = right coronary ostium, **LCO** = left coronary ostium, **RAS** = right aortic annulus, **NCAS** = non-coronary aortic sinus, **LAS** = left aortic annulus

(b) Late coronary stenosis

Coronary artery stenosis is a recognised late complication of AVR in 1% to 5% in patients occurring after one to six months after the procedure (Zaikas *et al.,* 2010). Coronary ostial stenosis can be caused by a widespread intimal thickening and fibrosis of the ostial margins which has been attributed to the healing process following micro-injuries secondary to cannulation (Yates *et al.,* 1973). The stenosis has also been attributed to intimal proliferation which in turn is caused by the turbulent flow of blood in the aorta and coronary arteries viz. 'ventricularization' of coronary flow that occurs after AVR (Rath *et al.,* 1988).

2.6.5 TRANSCATHETER AORTIC VALVE IMPLANTATION

Transcatheter aortic valve implantation (TAVI) is a technique which enables doctors to replace the aortic valve without surgically opening up the chest or cardiopulmonary bypass (Thomas and Mabin, 2012). The first TAVI procedure was first performed by Alain Cribier in 2002 in France specifically for the treatment of patients with aortic stenosis who were not able to withstand open surgery (Cribier *et al*., 2002). A significant number of patients with aortic valve disease are unable to withstand AVR due to advanced age, left ventricular failure and other medical conditions (Iung *et al*., 2005). TAVI has managed to cater for high risk patients. The procedure involves insertion of a self–expanding or balloon expandable bioprosthetic valve through a catheter and implanted within the diseased native aortic valve (Thomas and Mabin, 2012).

Although the procedure has been deemed safer than AVR in high risk patients, it has its own share of complications. According to Leon *et al*. (2010), TAVI is associated with higher risks of stroke than AVR in the post-operative period. It is also associated with coronary artery obstruction, though at lower rate than AVR (1% vs 3-5%) (Ribeiro *et al.,* 2013; Zaikas 2010). In a study by Ribeiro *et al*. (2013) that retrospectively analysed 24 patients who presented with coronary artery obstruction after TAVI, it was revealed that in 90% of the cases, the LCO was involved.

2.7 CLINICAL RELEVANCE

The aim of AVR is to reduce pressure and volume overload on the left ventricle, relieve symptoms thereby improving survival (Kulik *et al*., 2007). The procedure is indicated for aortic stenosis and regurgitation. Aortic stenosis is related to calcification, rheumatic heart disease, degeneration and bicuspid valves (Kumar and Clark, 2010). Aortic valve insufficiency is associated with rheumatic heart diseases, dilatation of the aortic root and rarely quadricuspid aortic valves (Zhu *et al*., 2013). The use of a small prosthesis in a narrow aortic root has been associated with increased pressure gradients, left ventricular outflow obstruction and therefore high morbidity and mortality (Ra mmos, 2006). To prevent this, there is a tendency to use 23 mm and larger prostheses (Kulik, 2007). In North America, surgeons routinely enlarge the aortic root using procedures such as Nick's, Manouguain and Ross' procedures to allow implantation of larger valves (David, 1999).

The incidence of narrow aortic roots among patients going for AVR surgery ranges from 7% (Borracci *et al.*, 2014) to 17% (Castro *et al.*, 2012). It is higher in women and patients with small BSA (Borracci *et al.*, 2014). Surgical aortic root enlargement is associated with increased operation time thus exposing the myocardium to hypoxic conditions for longer periods (Castro *et al.*, 2002). Some surgeons prefer 'shoe-horning', a technique described as forcing a larger size prosthesis into the aortic annulus without surgically enlarging the aortic root. However, 'shoe-horning' may distort the anatomy of the aortic root especially the coronary ostia with possible serious patho-physiological complications. Up to 5% of patients who undergo AVR may develop life-threatening coronary orifice stenosis (Zaikas *et al.,* 2010).

Transcatheter aortic valve implantation is now in use, especially with very ill patients who may be considered unfit for surgery (Cerillo, 2012). Intricate knowledge of the aortic root dimensions are essential to the surgeon for successful surgery. Aortic valve function has been shown to depend on the anatomic and dynamic relationship of the aortic valve and root (Bierbach *et al.*, 2010). Accurate knowledge of the location of coronary ostia is also of paramount importance for the success of procedures such as coronary angiography, angioplasty, coronary artery bypass grafting and coronary artery stenting (Kaur *et al*., 2012).

CHAPTER 3

MATERIALS AND METHODS

3.1 MATERIALS

3.1.1 SELECTED HEART SPECIMENS

Of the heart specimens examined (n=75), only 60 specimens met the inclusion criteria and were selected for the study. The cadaveric non-fixed heart specimens (n= 60) for this study were obtained during forensic post-mortem examinations at Gale Street State Mortuary, within the eThekwini Municipality, Durban, South Africa. Only adult hearts (age>18 years) were selected for this study. The heart specimens were divided into two cohorts viz. Group A and Group B. (1) Group A specimens (n=30) were used for the investigation of normal morphometry of the aortic root and left coronary ostium (LCO). (2) Group B (n=30) were used in the experimental study to determine the effect an oversized aortic valve prosthesis may have on the morphology and morphometry of the LCO. The procedure was a simulation of the 'shoe horning' technique employed to implant a large size valve in a narrow aortic root. Of these 30 specimens, 15 hearts were used in a further experimental study to investigate and compare pliability of the aortic root at the annulus and sino-tubular junction. The study was conducted at Gale Street State Mortuary. Ethical approval for the study was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Committee (Ethics number BE 307/15). The heart specimens were obtained during routine post mortem procedures. No tissue was removed from the samples. All measurements were done using a mathematical divider and a millimetre ruler. Measurements were rounded off to the nearest half (0.5) millimetre.

3.2 METHODS

The heart specimens were divided into two groups as mentioned above. (1) Group A cohort for the investigation of morphology and morphometry of the aortic root and left coronary ostium. (2) Group B for investigation of the changes associated with placing an oversized prosthesis in a normal aortic root.

3.2.1 ASSESSMENT OF GROUP A SPECIMENS: NORMAL AORTIC ROOTS

(a) Diameters of the aortic root

A total of 30 post mortem heart specimens were evaluated for aortic root morphometry. The internal aortic diameters at the level of the aortic annulus and sino-tubular junction were measured using a mathematical divider and a millimetre ruler (Figure 25). A callipers with a Vernier scale could not be used as this study was conducted in a state mortuary where unhygienic conditions prevailed.

(b) Morphology and morphometry of the LCO

The shape and diameter (Plate 1) of the LCO was measured. The distance (Plate 2) of the lower border of the LCO to the bottom of the left aortic sinus (aortic annulus) was measured. All measurements were taken three times and the average was calculated and recorded for analysis. An observer corroborated the results.

(c) Demographic data

The subjects' age, sex, race and height were recorded as well. The subjects were then analysed in different age cohorts of 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 and 90+ years following the method used by Devereux *et al*. (2012) and Son *et al*. (2013). The subjects were also divided into different height cohorts of 150-159 cm, 160-169 cm, 170-179 cm, 180-189 cm following methods used by Devereux *et al*. (2012).

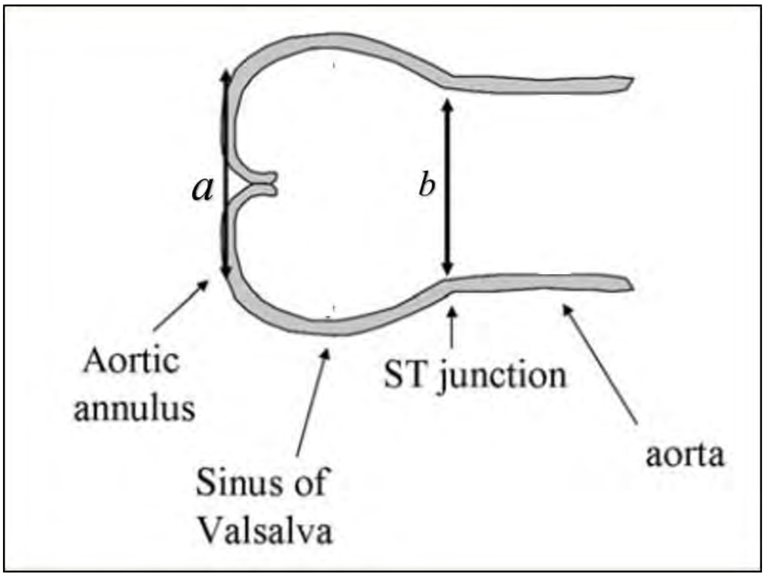

Figure 25: *An illustration showing the diameters of the aortic root measured at the aortic annulus (a) and sino-tubular junction (b) (Adapted from Flachskampf et al., 2010)*

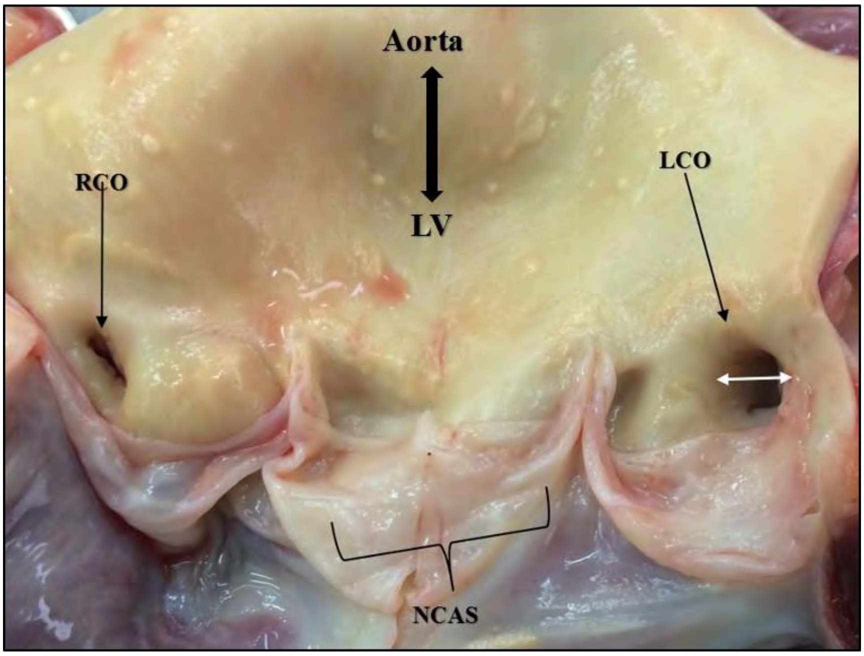

Plate 1*: The aortic root dissected open showing the diameter of the LCO.*

Key: **LCO** = Left coronary ostium, **RCO** = Right coronary ostium, **NCAS** = Non-coronary aortic sinus

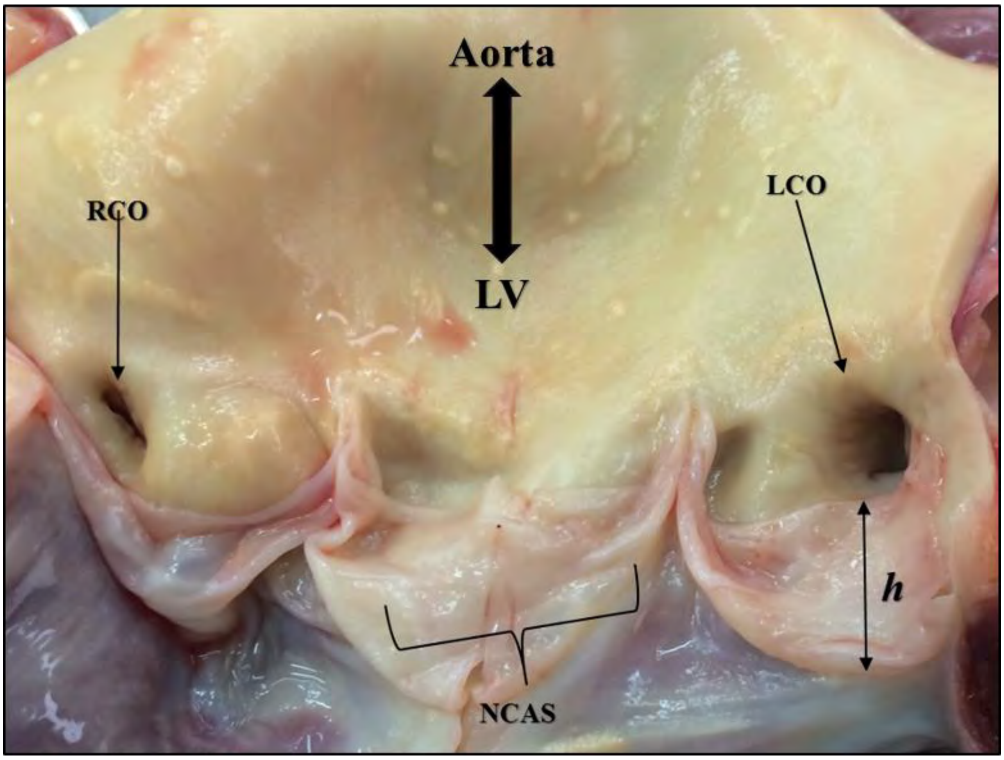

***Plate 2**: The aortic root dissected open showing the height (h) of the LCO from the bottom of the left aortic sinus.*

Key: **LCO** = Left coronary ostium, **RCO** = Right coronary ostium, **NCAS** = Non-coronary aortic sinus

3.2.2 ASSESSMENT OF GROUP B SPECIMENS: AORTIC VALVE REPLACEMENT

A total number of 30 cardiac specimens were evaluated to determine the anatomical changes associated with replacing an aortic valve with a mismatched prosthesis in a narrow aortic root. Normal heart specimens with normal aortic roots were used in this experimental study to simulate AVR in a narrow root. To observe the aortic root the upper two-thirds of the ascending aorta was truncated and cleared of any obstruction such as blood clots and tissue remains. The LCO was exposed and its shape noted. The shape of the LCO was described according to three reported shapes viz. circular, ellipsoid or crescentic (Govsa *et al.,* 2010). A mathematical divider was used to measure the diameter. The distance between the aortic annulus and the lower border of the LCO was recorded. After determining the normal diameter of the LCO, sizing of the aortic annulus followed. Using a guiding probe, aortic sizers of different diameters were inserted into the aortic root (the junction between the aortic valves and the beginning of ascending aorta) until the best fit was determined (Figure 26). The diameter of the fitting sizer for that heart was then recorded for analysis.

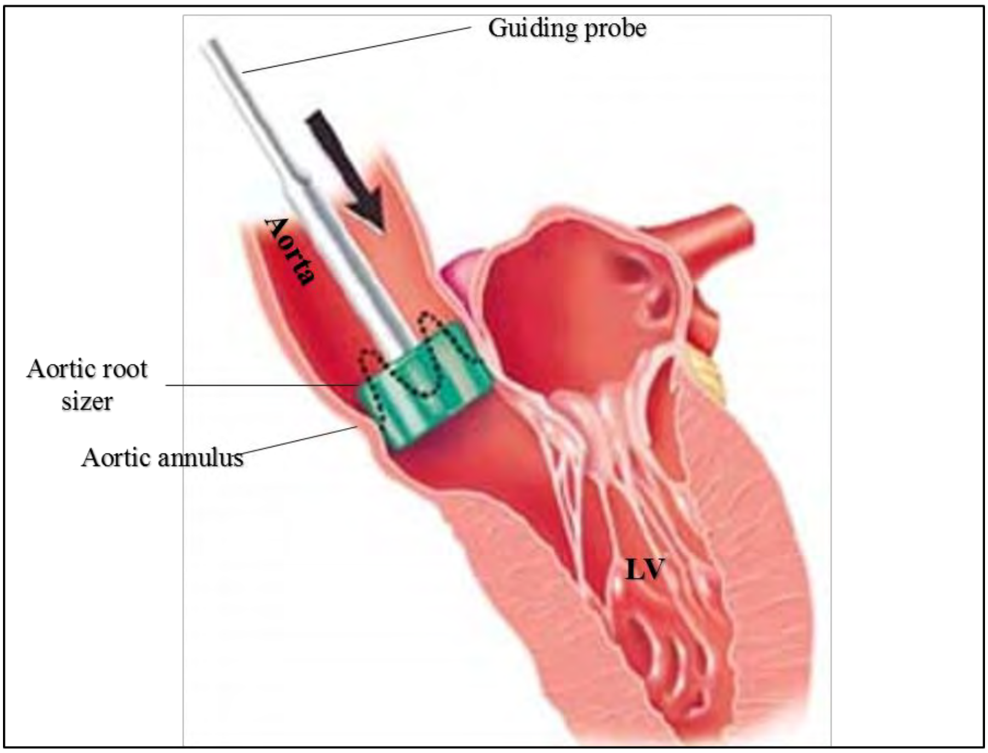

***Figure 26**: The procedure of sizing the aortic root. A probe with a sizer attached is inserted into the aorta to measure the size of the aortic annulus (Adapted from Ueda 2010)*

After measuring the diameter of the aortic annulus, an artificial valve (Figure 28) at 4 millimetres (two sizes larger) than the estimated diameter of the annulus was deliberately fitted into the annulus to simulate AVR in a narrow aortic root. The valve was sutured at the co mmissures and at the lowermost attachment of the valve cusps.

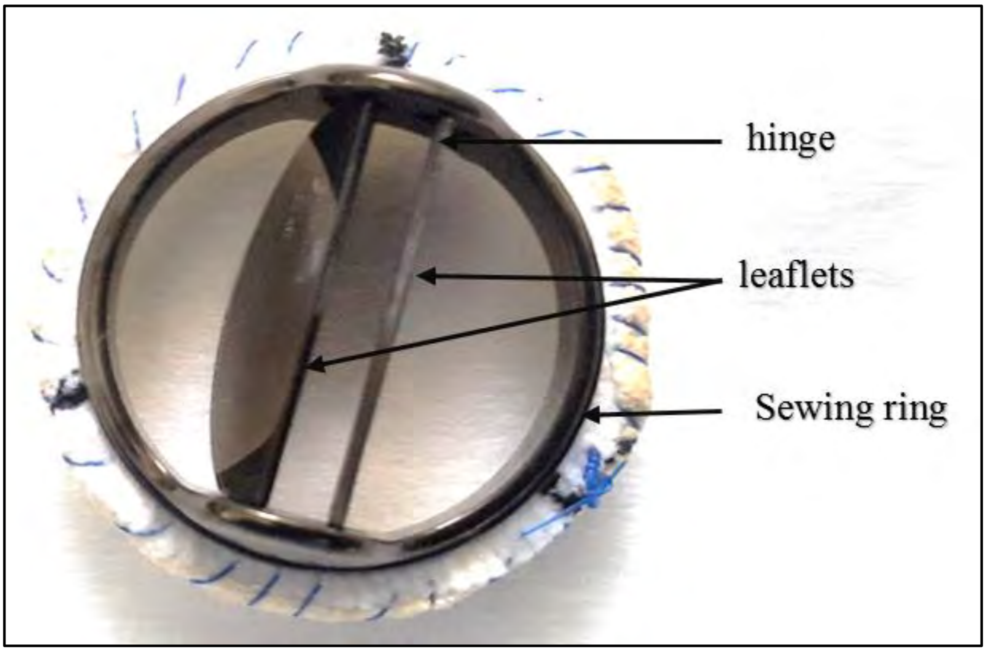

Plate 3*: St Jude mechanical valve size 25 mm*

With the larger valve fitted into place (assuming the position of the biological aortic valves), the vertical and horizontal diameters of the LCO were measured to determine if there were changes in diameter. The distance from the lower border of the LCO to the aortic annulus was also measured. The shape of the LCO was recorded. The artificial valve and the sutures were then removed and the cadaveric heart returned to the pathologists for further post-mortem analysis. The first two samples were done by an experienced cardio-thoracic surgeon who trained the researcher and a proper mechanical prosthetic valve, size 25 mm was used (Plate 3). The sewing ring of the prosthesis was sutured at the co mmissures between the non-coronary and left sinuses and between the left and right sinuses. More continuous suturing was performed along the scalloped lines of attachment of the valve leaflets up to the lowermost attachment of the left valve leaflet. All measurements were recorded three times and an independent observer corroborated results in 11 of the samples.

In 15 of these samples, the diameters of the aortic root at the annulus and at the sino-tubular junction were recorded using a divider and a millimetre ruler. The aortic annulus was stretched using surgical forceps and this dimension was also recorded. This was repeated at the sino-tubular junction level and the dimensions recorded. The change in diameter after stretching was recorded and expressed as a percentage.

3.3 STATISTICAL ANALYSIS

(a) Group A

The data collected was captured and analysed. A comparison between different ages, sex, height, ethnicity and aortic root size was made using the Statistical Package for Social Sciences (SPSS version 22.0) with the assistance of a biostatistician. The statistics used included the mean, range and standard derivation for each age interval. A 95% confidence level was adhered for all statistical tests.

(b) Group B

The results were subjected to analysis using SPSS version 22.0 for Windows 10. The results were then expressed as maximum, minimum, mean and standard deviation. The difference between the LCO diameters and heights before and after valve placement were determined using Student's t-tests and any significant correlation were identified using Pearson's correlation test. Any significant association was assumed at $p<0.05$.

The results of pliability tests at the aortic annulus and the sino-tubular junction were expressed as changes in normal diameter after stretching the aortic root. The two means were compared using Student's t-test and any significant correlations were identified using Pearson's correlation test. Any significant association was assumed at $p<0.05$.

3.4 ETHICAL CONSIDERATION

Ethical approval was acquired from the Biomedical Research and Ethics Co mmittee of University of KwaZulu-Natal (BREC No 307/15). Gatekeeper's permission and approval was sought and provided from the Chief Specialist of Forensic Pathology Services, Gale Street State Mortuary. The data obtained remained confidential and anonymous during and after the study.

CHAPTER 4

RESULTS

4.1 SAMPLE DEMOGRAPHICS

Of the post mortem hearts reviewed (n=75), 60 hearts met the inclusion criteria and were selected for the study. The heart specimens were grouped into two viz. (1) Group A and Group B. Group A specimens (n=30) were used for the investigation of normal morphometry of the aortic root and LCO and the influence of sex, height, age and race. (2) Group B specimens (n=30) were used for the experimental study to determine how an oversized aortic valve prosthesis can distort morphology and morphometry of the LCO. Of these 30 samples, 15 hearts were used to investigate and compare pliability of the aortic root at the annulus and sino-tubular junction.

4.2 GROUP A: NORMAL AORTIC ROOT

4.2.1 SAMPLE DEMOGRAPHICS

In this group, 30 normal post mortem hearts were analysed for the morphometric variations in the aortic root and LCO. The variations were cross tabulated with demographic characteristics and any significant associations were reported. Of the 30 specimens assessed, 63.3% ($^{19}/_{30}$) were males, whilst 36.7% ($^{19}/_{30}$) were females. With regard to race distribution, 63.3% [$^{19}/_{30}$] were indigenous Black Africans, 23.3% [$^{7}/_{30}$] were Indians and 13.3% [$^{4}/_{30}$] were White (Table 9).

***Table 9**: Demographic distribution of the Group A specimens*

Sex	Black	Indian	White	Total
Male	12	3	4	19
Female	7	4	0	11
Total	19	7	4	30

All the hearts analysed were obtained from adult cadavers with a mean age of 47.9 years [range 23- 90 years]. The frequency of specimens was 16.7% ($^{5}/_{30}$), 26.7% ($^{8}/_{30}$), 20% ($^{6}/_{30}$), 10% ($^{3}/_{30}$), 10% ($^{3}/_{30}$), 10% ($^{3}/_{30}$), 3.3% ($^{1}/_{30}$) and 3.3% ($^{1}/_{30}$) in the age groups of 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 and above 90 years, respectively (Figure 27).

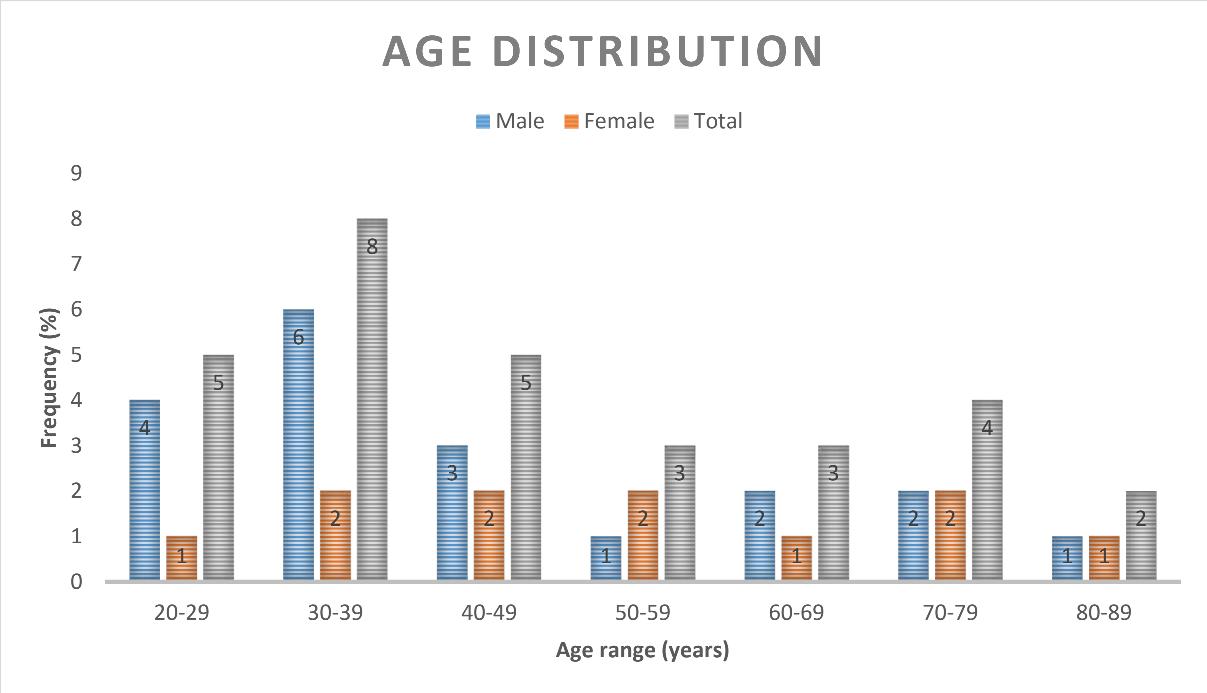

***Figure 27**: The frequency distribution of ages in the sample group (n=30)*

4.2.2 AORTIC ROOT DIAMETERS

(a) Aortic annulus diameters

The mean aortic annulus diameter in the study group (n=30) was 20.2 ± 2.1 mm. The smallest and largest diameter at the aortic annulus was 15.7 and 23.8 mm, respectively.

(b) The aortic diameter at sino-tubular junction

The mean diameter at the aortic annulus was 21.8 ± 2.3 mm. The largest diameter recorded was 26.5 mm and smallest diameter was 17.8 mm.

4.2.3 THE AORTIC ROOT DIAMETERS IN RELATION TO SEX

(a) Aortic annulus diameter

The mean aortic annulus diameter was 20.2 ± 2.3 mm for males and 20.1 ± 1.9 mm for females. There was no significant difference in the means of aortic annulus diameter between males and females (*p* = 0.85) (Table 10).

(b) The aortic diameter at the sino-tubular junction

The mean diameter at the sino-tubular junction was 21.8 ± 2.7 mm and 21.6 ± 1.9 mm for males and females respectively. There was no statistically significant difference in the diameter of the sino-tubular junction between males and females (*p* value = 0.72) (Table 10).

Table 10*: The frequency distribution of aortic annulus and sino-tubular junction diameter in male and females*

Part of the aortic root	Sex	Mean diameter (mm)	P value
Aortic annulus	Male	20.2	0.85
	Female	20.1	
Sino-tubular junction	Male	21.8	0.72
	Female	21.6	

4.2.4 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO RACE

The samples were derived from 19 Black Indigenous, 7 Indian and 4 white South Africans. The selection was based on availability of normal post mortem hearts at the mortuary.

(a) Aortic annulus diameter

The mean aortic annulus diameter was 20.3 ± 2.0 mm, 19.6 ± 2.1 mm and 21.0 ± 1.3 mm in Blacks (n=19), Indians (n=7) and Whites (n=4), respectively. There was no statistically significant difference in the aortic annulus diameter among different racial groups ($p = 0.35$) (Table 11).

(a) Sino-tubular diameter

The mean aortic annulus diameter was 22.0 ± 2.7 mm, 21.0 ± 3.0 mm and 22.3 ± 1.3 mm in Blacks (n=19), Indians (n=7) and Whites (n=4), respectively. There was no statistically significant difference in sino-tubular junction diameter among racial groups ($p = 0.58$) (Table 11).

Table 11*: Mean aortic annulus and sino-tubular junction diameters in different racial groups.*

Part of the aortic root	Race	Mean diameter (mm)	P value
Aortic annulus	Black	20.3±2.0	0.35
	Indian	19.6±2.1	
	White	21.0±1.3	
Sino-tubular junction	Black	22.0±2.7	0.58
	Indian	21.0±3.0	
	White	22.3±1.3	

4.2.5 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO HEIGHT

In assessing the influence of height of individuals on the aortic root diameters, the subjects were divided into height cohorts of 150-159 cm, 160-169 cm, 170-179 cm and 180 cm+ height groups.

(a) Aortic annulus diameter

The mean diameter at the aortic annulus was 19.5±2.4 mm, 20.1±2.2 mm, 20.0±2.1 mm and 21.9±1.7 mm for the 150-159 cm, 160-169 cm, 170-179 cm and 180 cm+ height groups (Table 11).

(b) Diameter of the aortic root at the sino-tubular junction

The mean diameter at the aortic annulus was 21.4±3.2 mm, 21.7±2.4 mm, 21.6±1.8 mm and 23.7±2.5 mm for the 150-159 cm, 160-169 cm, 170-179 cm and 180 cm+ height groups (Table 12).

Table 12*: Frequency of aortic annulus and sino-tubular junction diameter in different height groups.*

Height group (cm)	**150-159**	**160-169**	**170-179**	**180-189**
Sample size (n)	4	13	10	3
Mean Aortic annulus diameter (mm)	19.5±2.4	20.1±2.2	20.0±2.1	21.9±1.7
***p* value**	0.364			
Mean sino-tubular junction diameter (mm)	21.4±3.2	21.7±2.4	21.6±1.8	23.7±2.5
***p* value**	0.389			

4.2.6 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO AGE

In assessing the influence of age of individuals on the aortic root diameters, the subjects were dived into age cohorts of 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80-89 years, 90+ years.

(a) Aortic annulus diameter

The mean aortic annulus diameter was 17.8 ±1.6 mm, 19.3 ± 1.1 mm, 20.7 ±2.1 mm, 21.9 ±0.4 mm, 22.6 ±2.0 mm, 19.7 ±2.4 mm, 19.2 mm and 23.3 mm in the age group of 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90+ years, respectively. There was significant correlation between age and aortic annulus diameter (*p*=0.03) (Table 13).

(b) The sino-tubular junction

The mean aortic annulus diameter was 19.5 ±0.9 mm, 21.0 ± 1.1 mm, 22.4 ±2.4 mm, 23.0 ±0.3 mm, 24.7 ±2.6 mm, 21.0 ±2.8 mm, 21.8 mm and 26.5 mm in the age group of 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90+ years, respectively. There was significant correlation between age and aortic annulus diameter (*p*=0.03) (Table 13).

***Table 13**: The mean aortic annulus and sino-tubular diameter in different age groups*

Age (years)	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**80-89**	**90+**
Sample size (N)	5	8	6	3	3	3	1	1
Mean aortic annulus diameter (mm)	17.9± 1.5	19.5±1.2	20.7±2.1	21.9±0.4	22.6±2.0	19.7±2.4	19.2	23.3
***p* value**	**0.03**							
Mean aortic annulus diameter (mm)	19.5±0.9	21.0±1.1	22.4±2.4	23.0±0.3	24.7±2.6	21.0±2.8	21.8	26.5
***p* value**	**0.01**							

4.2.7 THE RELATIONSHIP BETWEEN DIAMETER AT THE AORTIC ANNULUS AND SINO-TUBULAR JUNCTION

The observed aortic annulus diameters and diameter of the aortic root at the sino-tubular junction showed a significant correlation (*p* value = 0.00) (Figure 28). There was an observed constant increase of the sino-tubular diameter when the aortic annulus diameter increased.

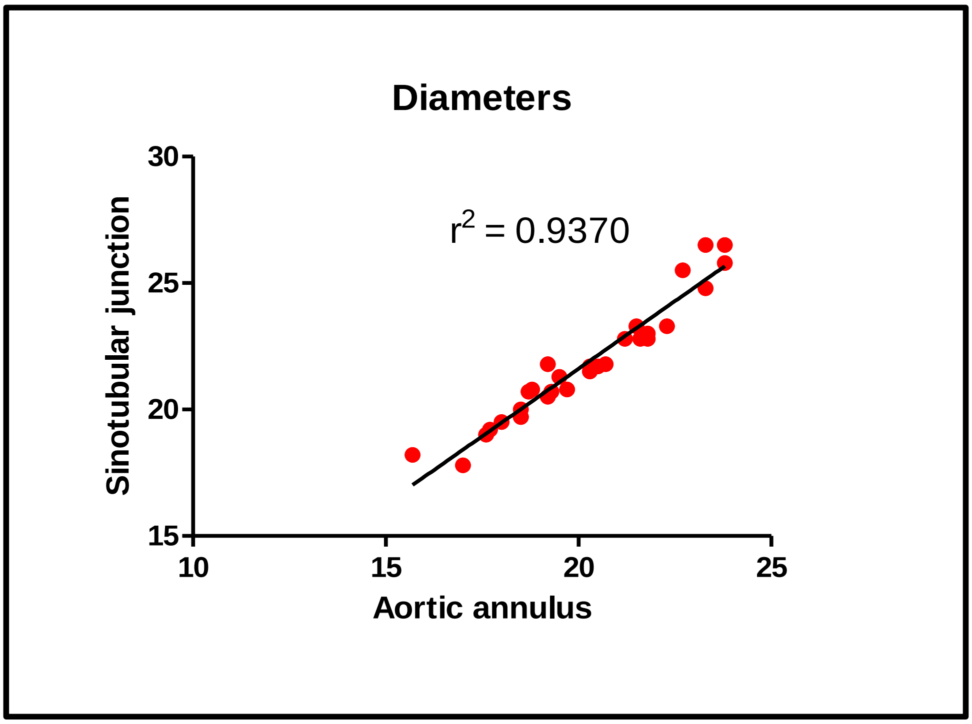

Figure 28*: The graph illustrates the relationship between the diameters of the aortic annulus and the sino-tubular junction.*

Using regression analysis (regression coefficient; r^2= 0.937), the diameter of the aortic annulus was 93.7% of the observed diameter of the sino-tubular junction.

4.3 THE LEFT CORONARY OSTIUM

The shape, position and size of the left coronary ostia was analysed in 30 heart specimens.

4.3.1 SHAPE OF THE LEFT CORONARY OSTIUM (LCO)

For the hearts analysed, 96.7% ($^{29}/_{30}$) of the left coronary ostia were circular whilst 3.3% ($^{1}/_{30}$) were ellipsoid (Table 14) (Plates 4 and 5).

***Table 14**: Frequency of the different types of left coronary ostia shapes*

Shape of LCO	Frequency	Percent (%)
Oval	29	96.7
Ellipsoid	1	3.3
Total	30	100.0

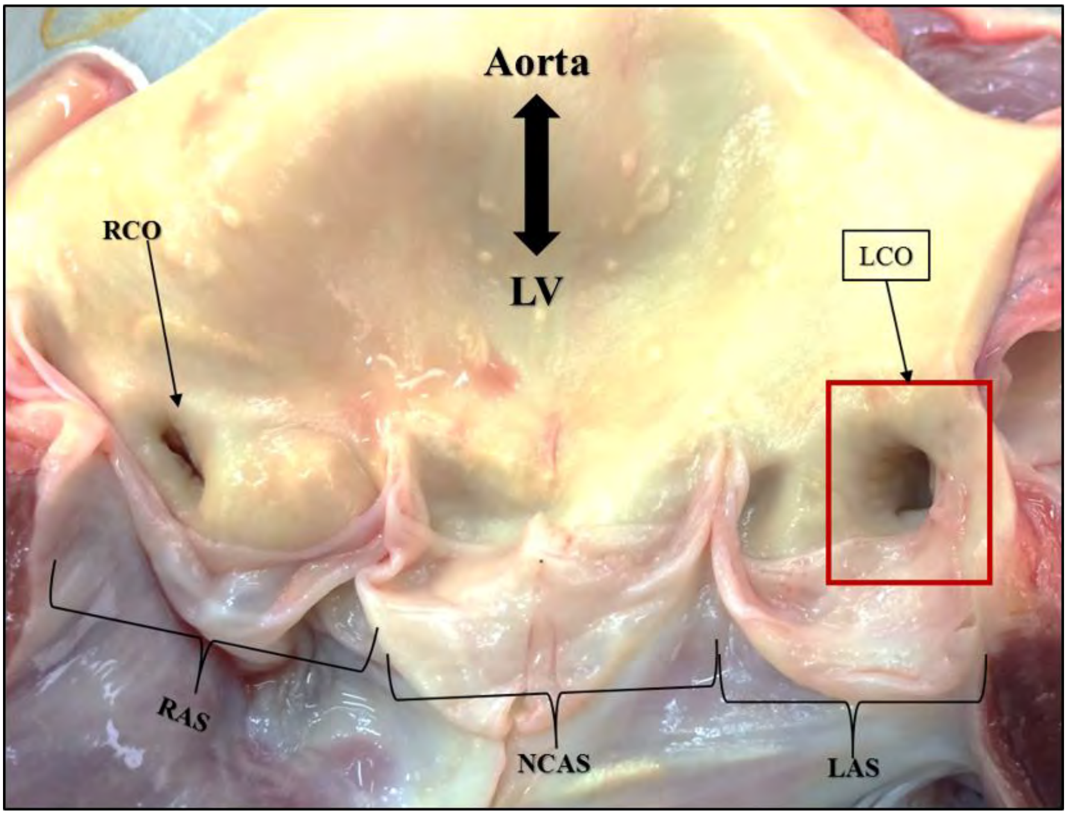

***Plate 4**: The aortic root exposed showing a circular shaped LCO*

Key: LCO= Left coronary ostium, **RCO** = Right coronary ostium, **RAS** = Right aortic sinus, **NCAS** = Non-coronary sinus, **LAS** = Left aortic sinus, **LV** = Left ventricle

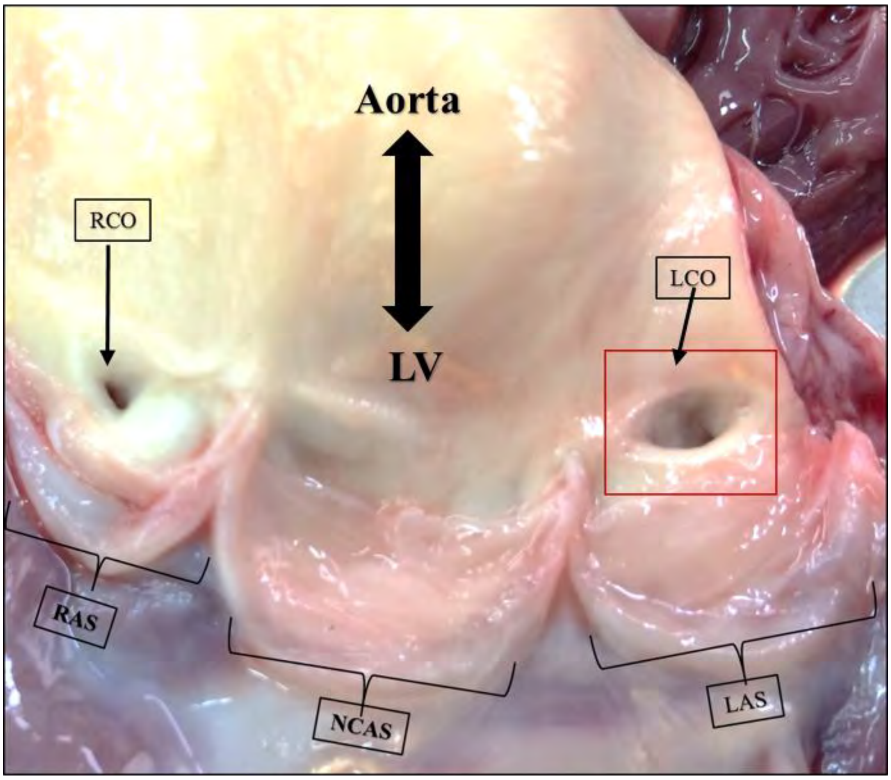

Plate 5*: The aortic root exposed to show an ellipsoidal shaped LCO*

Key: LCO= Left coronary ostium, **RCO** = Right coronary ostium, **RAS** = Right aortic sinus, **NCAS** = Non-coronary sinus, **LAS** = Left aortic sinus, **LV** = Left ventricle

4.3.2 POSITION OF THE LCO

All the LCO were located within the appropriate left aortic sinus. The LCO was located below, on and above the sino-tubular junction in 73.3% ($^{22}/_{30}$), 23.3% ($^{7}/_{30}$) and 3.3% ($^{1}/_{30}$), respectively (Figure 29) (Plates 6-8).

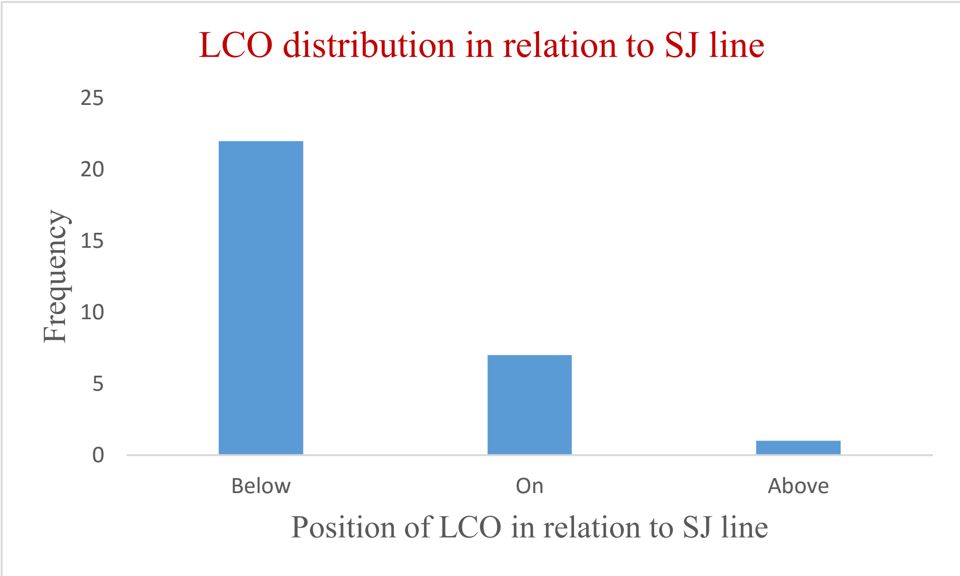

Figure 29*: Frequency distribution of the positions of LCO in relation to SJ line*

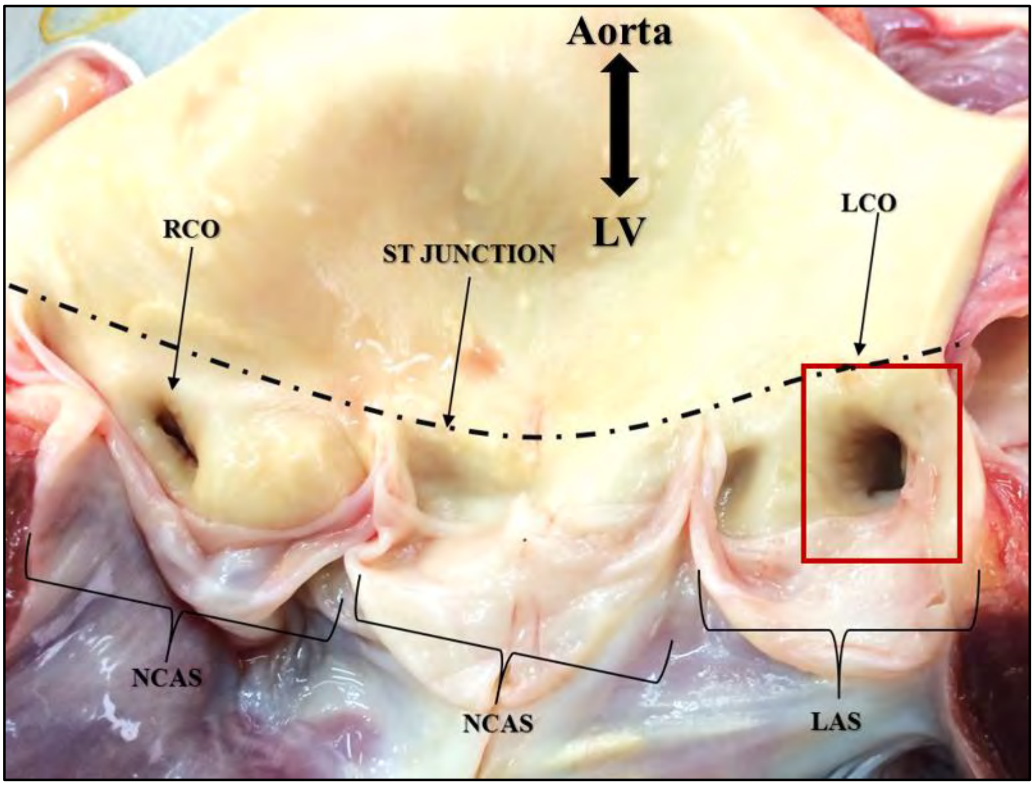

Plate 6*: The aortic root exposed showing the LCO below the sino-tubular line. The dashed line shows the position of the sino-tubular line*

Key: LCO= Left coronary ostium, **RCO** = Right coronary ostium, **RAS** = Right aortic sinus, **NCAS** = Non-coronary sinus, **LAS** = Left aortic sinus, **LV** = Left ventricle

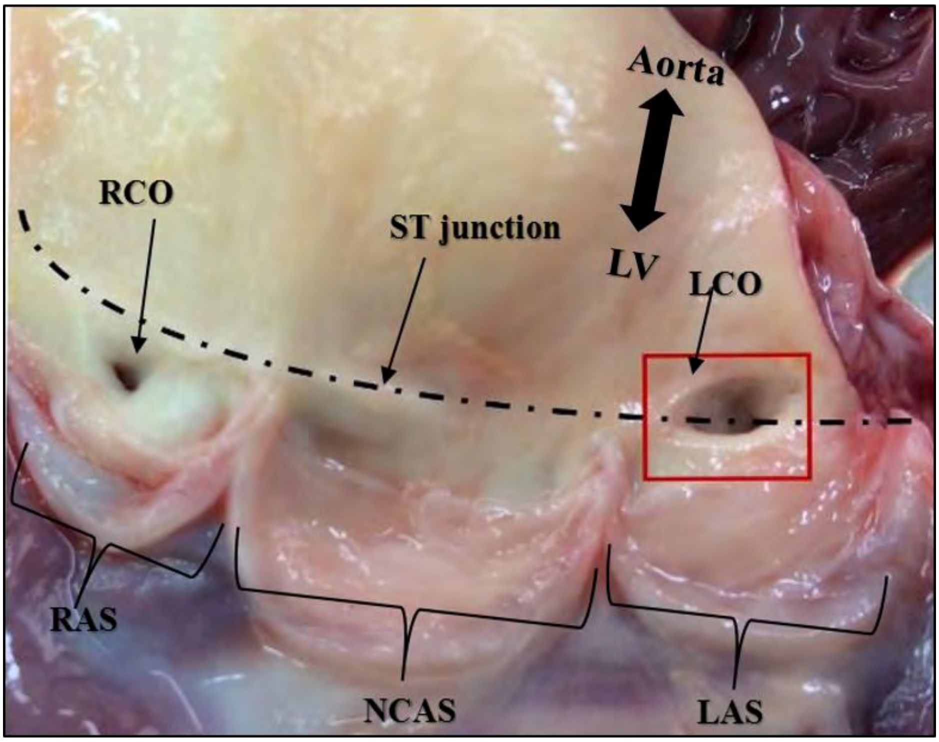

Plate 7*: The aortic root exposed showing the LCO* **on** *the sino-tubular line. The dashed line shows the position of the sino-tubular line.*

Key: LCO= Left coronary ostium, **RCO** = Right coronary ostium, **RAS** = Right aortic sinus, **NCAS** = Non-coronary sinus, **LAS** = Left aortic sinus, **LV** = Left ventricle

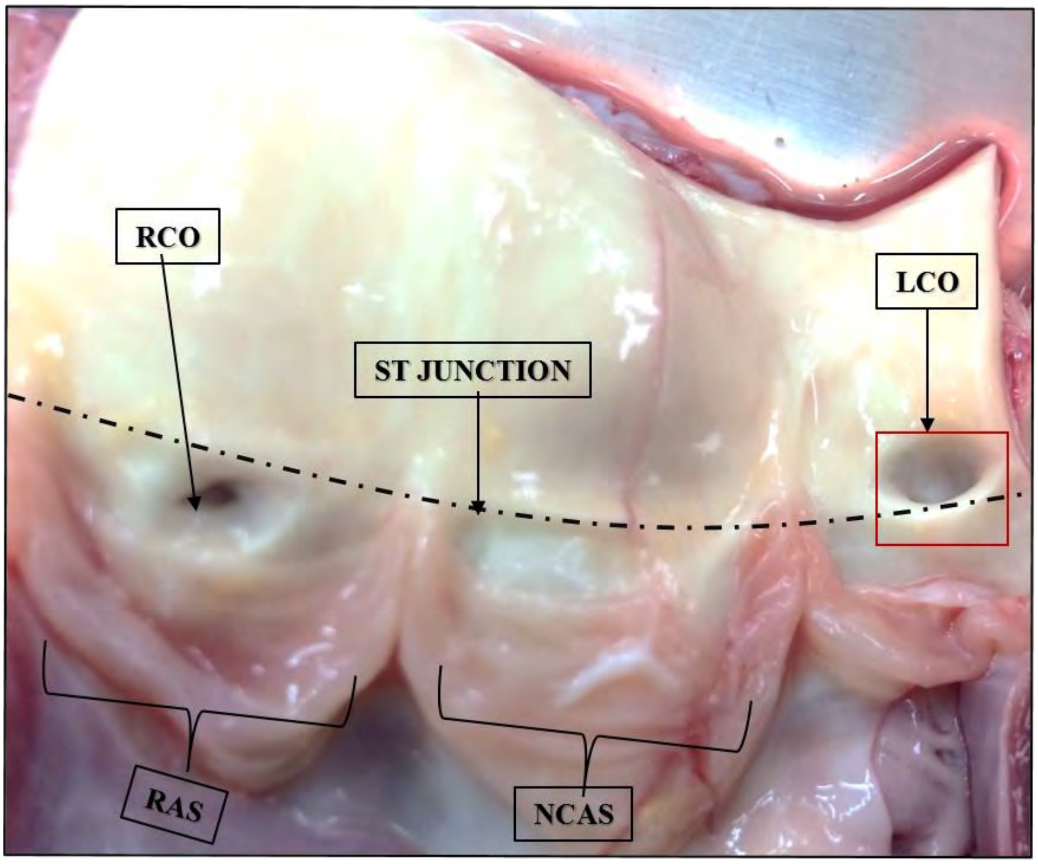

Plate 8*: The aortic root exposed showing the LCO* ***above*** *the sino-tubular line. The dashed line shows the position of the sino-tubular line.*

Key**: LCO**= Left coronary ostium, **RCO** = Right coronary ostium, **RAS** = Right aortic sinus, **NCAS** = Non-coronary sinus, **LAS** = Left aortic sinus

4.3.3 HEIGHT OF LCO FROM AORTIC ANNULUS

The height of the LCO from the bottom margin of the left aortic sinus was analysed. The mean height was 12.8 ± 2 mm. The minimum height recorded was 9.7 mm whilst the maximum was 18.0 mm (Plate 9).

(a) The height of the LCO from the aortic annulus in relation to sex

The mean height of the LCO was 13.2 ± 2.1 mm and 11.6 ± 1.8 mm in males (n=19) and females (n=11), respectively. There was no statistically significant difference in height of LCO between males and females ($p = 0.327$) (Table 15).

(b) The height of the LCO from the aortic annulus in relation to race

The mean height of the LCO was 12.7 ± 2 mm in Black Indigenous South Africans (n=19), 12.8±2.1 mm in Indians (n=7) and 13.4 ± 1.5 mm in Whites (n=4). There was no significant difference in height of LCO from aortic annulus in different racial groups ($p = 0.821$) (Table 15).

(c) The height of the LCO from the aortic annulus in relation to age

The mean distance of LCO from the aortic annulus was 12.5 ±1.9 mm, 13.1 ±2.5 mm, 12.4 ±1.0 mm, 13.2 ±2.5 mm, 15.8 mm and 15.5 mm for the age group 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 and 90 +years respectively. There was no correlation between the height of the LCO from the aortic annulus and age ($p = 0.318$) (Table 15).

(d) The height of the LCO from the aortic annulus in relation to height of subjects

The mean distance of the LCO from the aortic annulus was 12.4 ±2.2 mm, 12.9 ±2.0 mm, 12.3 ±1.2 mm and 14.7 ±2.7 mm for individuals whose height are in the range of 150-159c mm, 160-169 cm, 170-179 cm and 180+ cm, respectively. There was no significant relationship between the height of the LCO and the height of individual subjects (p = 0.339) (Table 15).

Table 15: *The mean heights of the LCO from aortic annulus in different sexes, races, age groups and heights groups.*

	Sex	**N**	**Mean ±Std. Dev**	***p* value**
Height of LCO (mm) from Aortic Annulus	Male	19	13.2 ±2.1	0.327
	Female	11	11.6 ±1.8	
	Race	**N**	**Mean ±Std. Dev**	***p* value**
	Blacks	19	12.7±2.0	0.821
	Indian	7	12.8±2.1	
	White	4	13.4±1.5	
	Age group (years)	**N**	**Mean ±Std. Dev (mm)**	***p* value**
	20-29	5	12.5±1.9	0.318
	30-39	8	13.1±2.5	
	40-49	6	12.4±1.0	
	50-59	3	13.2±1.8	
	60-69	3	11.0±1.3	
	70-79	3	13.2±2.5	
	80-89	1	15.8	
	90+	1	15.5	
	Height group (cm)	**N**	**Mean ±Std. Dev (mm)**	***p* value**
	150-159	4	12.4±2.2	0.339
	160-169	13	12.9±2.0	
	170-179	10	12.3±1.2	
	180+	6	14.7±2.7	

4.3.4 THE DIAMETER OF LCO

The mean diameter of the LCO was 6.1 ± 1.3 mm in all of the heart specimens (n=30). The largest diameter was 8.8 mm and the smallest diameter was 4.2 mm (Plate 10).

(a) ***The diameter of the LCO in relation to sex***

The mean diameter of the LCO was 6.5± 1.4 mm and 5.4 ± 0.8 mm in males (n=19) and females (n=11), respectively. The difference between the two diameters in males and females was statistically significant (p = 0.009) (Table 16).

(b) The diameter of the LCO in different racial groups

The mean diameter of the LCO was 5.9 ± 1.0 mm, 6.2 ± 1.9 mm and 6.4 ± 1.3 mm in Black Indigenous South Africans (n=19), Indians (n=7) and Whites (n=4), respectively. The difference in diameter of the LCO in the three different racial groups was not statistically significant (p= 0.775) (Table 16).

(c) The diameter of the LCO in relation to age

The mean diameter of the LCO was 5.5 ±0.9 mm, 6.2 ±1.5 mm, 6.2 ±1.4 mm, 6.1 ±1.7 mm, 6.9 ±1.4 mm, 5.3 ±1.3 mm, 5.8 mm and 6.8 mm for the age group of 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 and 90+ years, respectively. There was no significant relationship between LCO diameter and age of individuals (Table 16).

(d) The diameter of the LCO in relation to height of individuals

The mean diameter of the LCO was 5.4 ±0.8 mm, 5.7 ±1.1 mm, 8.1 ±2.9 mm and 7.2 ±1.7 mm for the individuals whose height was in the range of 150-159 cm, 160-169 cm, 170-179 cm and 180+ cm, respectively. There was statistically a significant correlation between the diameter of the LCO and height of the individuals ($p = 0.04$) (Table 16).

Table 16*: The diameter of the LCO in different sexes, races, age groups and height groups.*

	Sex	**N**	**Mean ±Std. Dev**	***p* value**
Diameter of LCO (mm)	Male	19	6.4±1.4	0.12
	Female	11	5.7±0.8	
	Race	**N**	**Mean ±Std. Dev**	***p* value**
	Blacks	19	5.9±1.0	0.775
	Indian	7	6.2±1.9	
	Blacks	4	6.4±1.3	
	Age groups (years)	**N**	**Mean ±Std. Dev**	***p* value**
	20-29	5	5.5±0.9	0.721
	30-39	8	6.2±1.5	
	40-49	6	6.2±1.4	
	50-59	3	6.1±1.7	
	60-69	3	6.9±1.4	
	70-79	3	5.3±1.3	
	80-89	1	5.8	
	90+	1	6.8	
	Height group (cm)	**N**	**Mean ±Std. Dev**	***p* value**
	150-159	4	5.4±0.8	0.025
	160-169	13	5.7±1.1	
	170-179	10	8.1±2.9	
	180+	6	7.2±1.7	

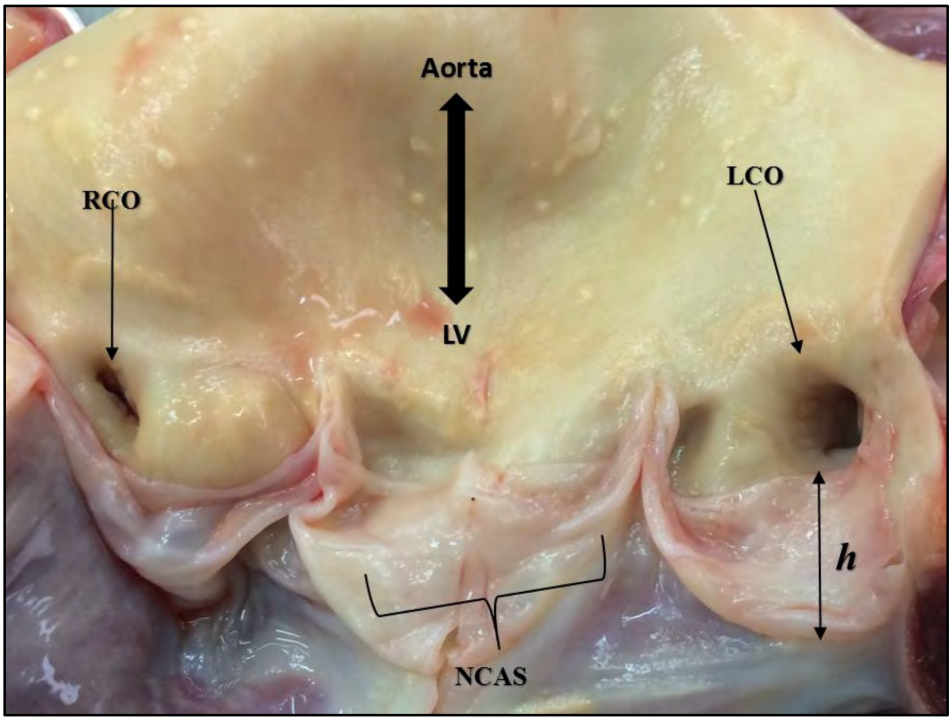

***Plate 9**: The aortic root dissected showing the process of measuring the height (**h**) of the left coronary ostium from the bottom of the sinus.*

Key: LCO = left coronary ostium, **RCO** = right coronary ostium, **NCAS** = Non-coronary aortic sinus, **LV** = Left ventricle, ***h* =** height of the LCO from the aortic annulus

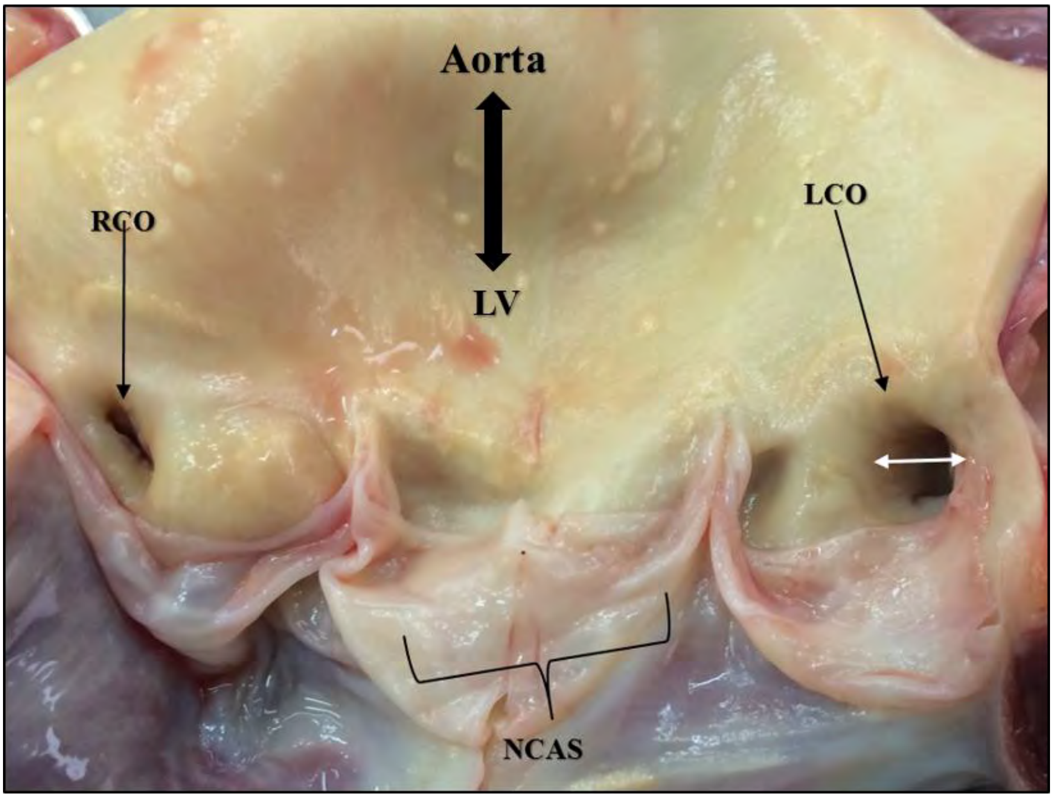

Plate 10*: The aortic root dissected showing the diameter of the left coronary ostium.*

Key: **RCO** = right coronary artery, **LCO** = left coronary ostium, **NCAS** = non-coronary aortic sinus, **LV** = Left ventricle

4.4 GROUP B: AORTIC VALVE REPLACEMENT

For group B specimens, 30 adult post mortem hearts with normal aortic roots were selected for the experimental study. The shape, diameter and height of the LCO from the aortic annulus before implantation of the prosthesis were observed. The same parameters were recorded after insertion of the prosthesis. The results were expressed as minimum, maximum, mean ± standard deviation and the frequency distribution was tabulated into percentiles. Significant associations were observed at a p-value<0.05 in all the groups.

4.4.1 CHANGES IN SHAPE OF THE LCO

It was observed that the shape of the LCO for this sample was circular in all (100%) specimens, before insertion of the prosthesis (Plate 11).

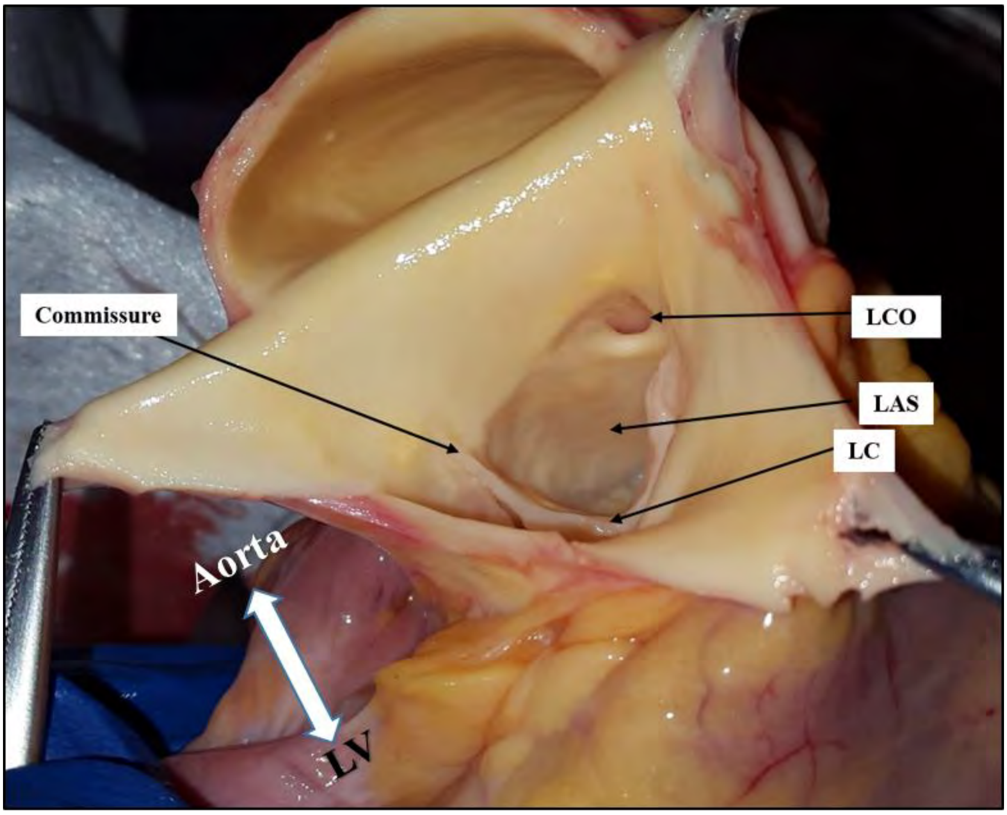

Plate 11: *Aortic root showing a circular LCO located within the left aortic sinus (LAS).*

Key: **LCO** = left coronary ostium, **LAS** = left aortic sinus, **LC** = left cusp, **LV** = Left ventricle

After insertion of the prosthesis, the shape of the LCO changed to ellipsoidal in all of the 30 specimens (Plate 12).

4.4.2 CHANGES IN DIAMETER OF LCO

The mean average diameter of the LCO was 4.8 ± 0.7 mm before insertion of the prosthesis. The minimum and maximum diameters observed were 3.3 and 6.2 mm respectively. After the prosthesis was inserted the shape changed from circular to ellipsoidal (Plates 13). The mean average vertical diameter was 1.6 ± 0.4 mm whilst the mean average horizontal diameter was 8.2 ± 0.6 mm. The minimum and maximum vertical diameters were 1.0 and 2.3 mm respectively. The minimum and maximum horizontal diameters were 7.0 and 9.3 mm respectively. There was significant difference (*p* value 0.00) between the normal diameter before prosthesis insertion and vertical diameter of the LCO after prosthesis was inserted. There was also significant associations (*p* = 0.00) between the normal diameter before prosthesis insertion and the horizontal diameter after prosthesis insertion (Table 17).

Table 17*: The mean diameters of LCO before and after insertion of the prosthesis*

	Before prosthesis implantation	**After prosthesis implantation**	***p* value**
Mean horizontal diameter (mm)	4.8	8.2	**0.00**
Mean vertical diameter (mm)	4.8	1.6	**0.00**
Mean height of LCO (mm)	11.8	5.3	**0.00**

4.4.3 CHANGES IN HEIGHT OF LCO FROM AORTIC ANNULUS

The mean distance of the lower edge of the LCO from the aortic annulus was 11.8 ± 1.9 mm. After the insertion of an oversized prosthesis, the mean distance was 5.3 ± 1.0 mm. There was a statistically significant change in the height of the LCO (*p* = 0.00) (Table 16). The mean change in height of LCO was 6.6 mm which represented a mean of 55.6% of the original mean height.

4.4.4 DISTORTION OF AORTIC WALL

After insertion of the prosthesis, a transverse ridge in the aortic wall was observed in all the specimens (100%) immediately above the coronary orifice to the extent that the LCO was almost covered. This ridge extended from the commissure between the non-coronary and left aortic sinuses to the commissure between the left and right aortic sinuses. It was located just above the LCO and it almost buried the orifice of the left coronary artery (Plate 12)

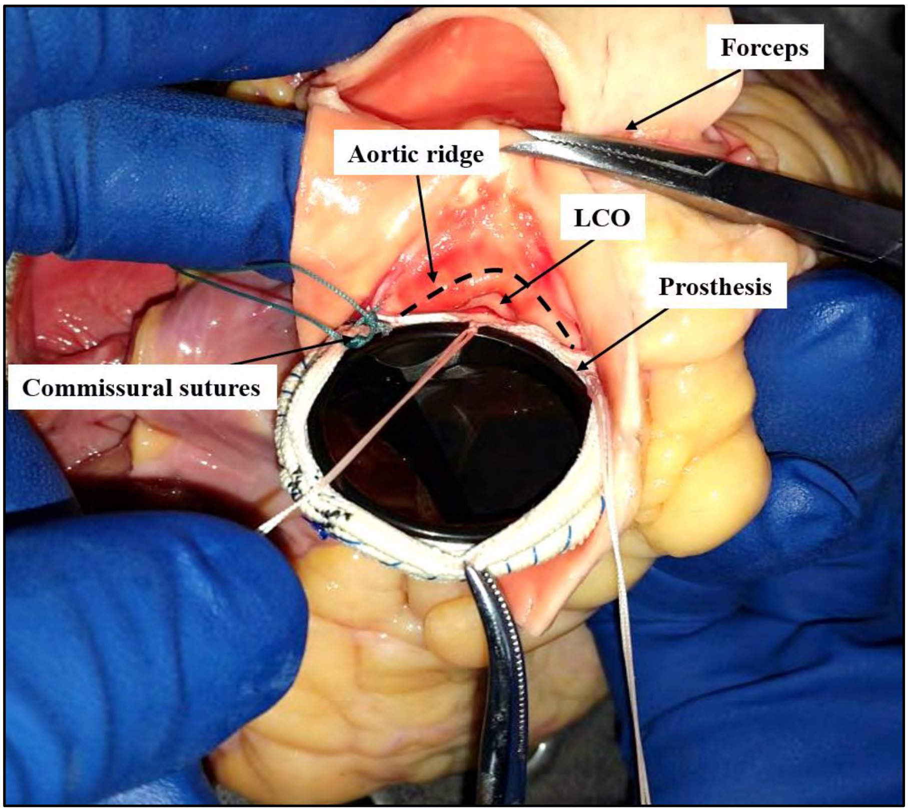

Plate 12: *Aortic root with a prosthesis in place. The shape of the LCO has changed to ellipsoidal and the dashed line illustrates a ridge that is formed above the LCO.*

***Key*: LCO** = left coronary ostium

4.5 PLIABILITY OF THE AORTIC ANNULUS AND SINO-TUBULAR JUNCTION

The pliability of the aortic root was defined as the capability of the aortic root wall to be stretched. The objective was determine the difference in pliability of the aortic annulus and the sino-tubular junction. Of the 30 heart specimens in Group B, 15 heart specimens were used for this aspect of the study. The diameters at the aortic annulus and the sino-tubular junction using a mathematical divider and a millimetre ruler. The measurements were rounded to half (0.5) a millimetre.

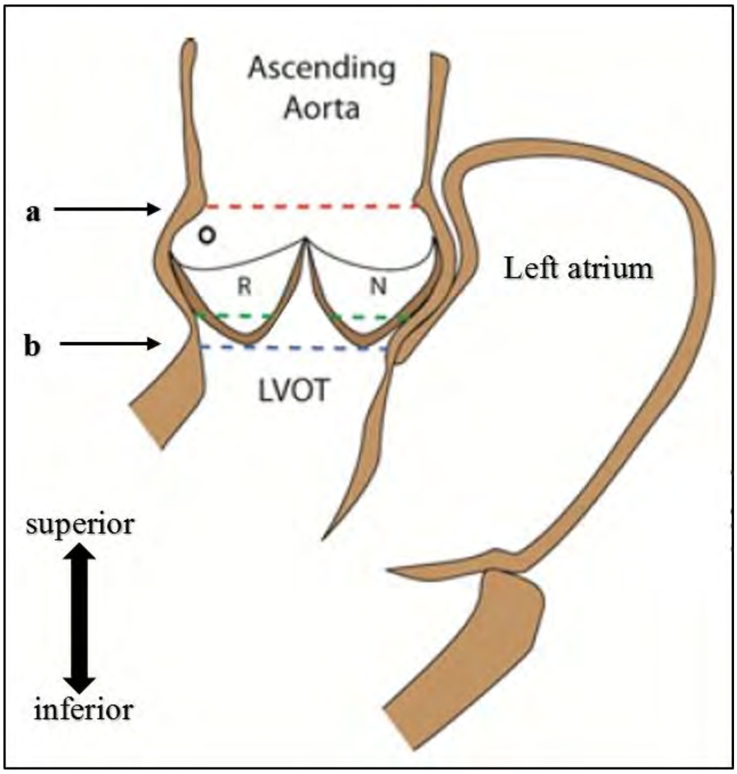

Figure 30: An illustration of the aortic root showing the two diameters measured at the level of the (a) aortic annulus and (b) sino-tubular junction
(Adapted from Zalkind et al., 2013)

KEY: **LVOT** = Left ventricular outflow tract

(a) Pliability of the aortic annulus

The mean diameter of the aortic annulus was 20.2 ± 2.2 mm. The minimum and maximum diameters were 17.3 mm and 23.8 mm respectively. After maximum stretching of the aortic annulus, the mean diameter was 37.9 ± 2.9 mm. The maximum and minimum diameter was 33.8 mm and 44.0 mm after maximum stretching. There was significant difference between normal aortic annulus diameter and the stretched diameter (*p* value =0.000). The mean difference between normal diameter and stretched diameters was 17.7 ± 2.1 mm and this represents the extent to which the annulus can be stretched. Pliability of the aortic annulus was assumed to be how much the aortic annulus could be stretched viz. the difference between normal and stretched diameters.

(b) Pliability of the sino-tubular junction

The mean diameter of the sino-tubular junction was 22.3 ± 2.5 mm. The minimum and maximum diameters were 18.2 mm and 27.2 mm respectively. After maximum stretching of the aortic annulus, the mean diameter was 49.9 ± 4.8 mm. The maximum and minimum diameter was 44.3 mm and 61.3 mm after maximum stretching. The difference between the normal mean aortic annulus diameter and the stretched diameter was statistically significant (*p* value =0.000). The mean difference between normal diameter and stretched diameters was 27.6 ± 3.1 mm and this represented the extent to which the sino-tubular junction could be stretched viz. the pliability of the sino-tubular junction.

(c) The differences in pliability of aortic annulus and sino-tubular junction

The mean increase in diameter after maximum stretching was 17.7 mm and 27.7 mm for the aortic annulus and sino-tubular junction respectively. The correlation between the mean increase in diameter at the aortic annulus and the mean increase in diameter at the sino-tubular junction was statistically significant (*p* value =0.015) (Table 18).

Table 18*: Pliability of the aortic annulus and sino-tubular junction*

<table>
<tr><th></th><th>Mean change in diameter (mm)</th><th>p value</th></tr>
<tr><td>Aortic annulus</td><td>17.7</td><td rowspan="2">0.00</td></tr>
<tr><td>Sino-tubular junction</td><td>27.7</td></tr>
</table>

The relationship between pliability at the aortic annulus and at the sino-tubular junction is shown in Figure 31. The relationship was summarised as

Pliability at sino-tubular junction = 15.2 + 0.669 x (pliability at aortic annulus)

The figure 15.2 represents the pliability of the sino-tubular junction when pliability at the aortic annulus is zero.

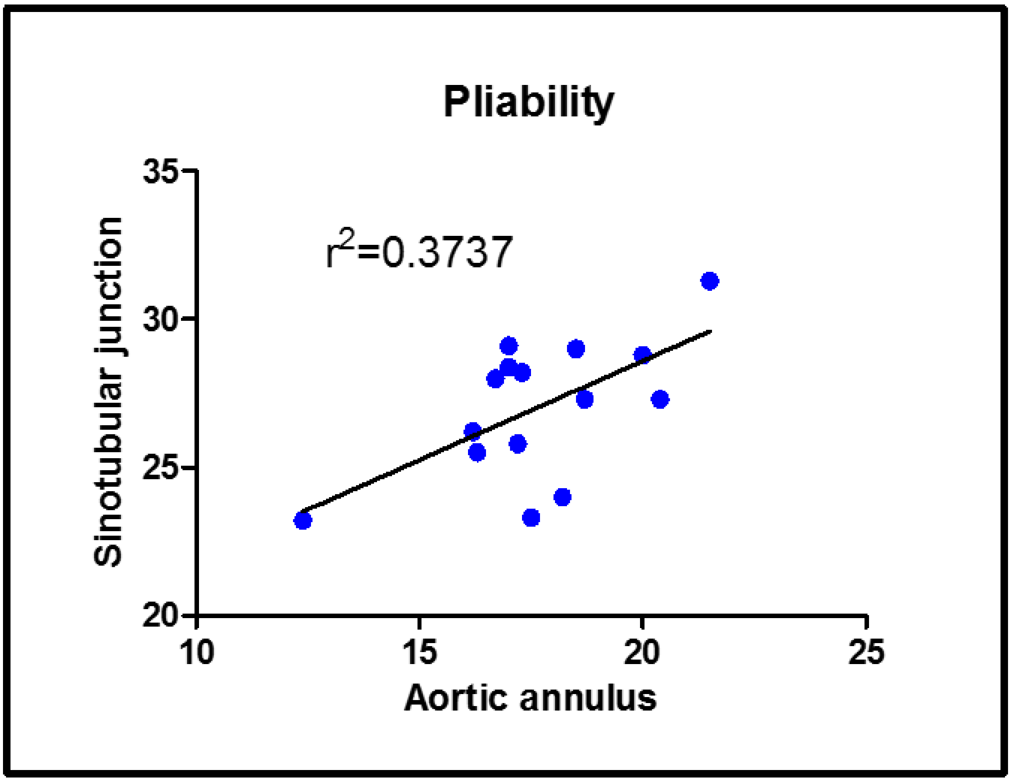

***Figure 31**: The relationship between pliability at the aortic annulus and sino-tubular junction*

The coefficient 0.669 is the gradient viz. change in pliability factor of aortic annulus to the sino-tubular junction.

Pliability factor of the aortic annulus = $\frac{pliability\ of\ the\ aortic\ annulus}{(pliability\ at\ the\ sinotubular\ junction)}$

Pliability factor of the sinobular line = $\frac{1}{pliability\ factor\ of\ the\ annulus\ to\ the\ sinotubular\ junction}$

$= \frac{1}{0.669}$

Pliability factor = 1.4947

= 1.5

For any change in diameter at the aortic annulus, the sino-tubular junction will change 1.5 times more. Hence, the sino-tubular junction is more pliable than the aortic annulus by a factor of 1.5.

4.6 SU MMARY OF RESULTS

4.6.1 AORTIC ROOT DIAMETERS

The mean aortic root diameters at the aortic annulus and the sino-tubular junction were. There was a significant relationship between the aortic root diameters and age of individuals.

4.6.2 MORPHOLOGY AND MORPHOMETRY OF LCO

The majority of LCO were circular in shape. Most (73.3%) of the LCO were located below the sino-tubular junction, whilst 23.3% were located on the sinotubular junction. Only 3.3% were located above the sino-tubular junction. Male subjects had a significantly larger LCO than females (6.5 *vs* 5.4 mm).

4.6.3 AORTIC VALVE REPLACEMENT

There was significant reduction in the height of the LCO from the bottom of the left coronary sinus after insertion of the prosthesis. The shape of the LCO changed significantly from circular shape to an ellipsoid or slit-like shape. This change was confirmed by significant changes in the vertical and horizontal diameters. A tight band of tissue was also formed just above the LCO which extended from the adjacent commissures.

CHAPTER 5

DISCUSSION

5.1 SAMPLE DISTRIBUTION

The present study was conducted to evaluate the aortic root morphometry and document the effect of implanting an oversized aortic valve prosthesis in the aortic root on the LCO. Coronary ostial obstruction has been reported more on the left than right coronary artery following both open surgery and TAVI. According to Ribeiro *et al*. (2013), the LCO is involved in 90% of coronary artery stenosis and it has been suggested that this could be related to the location of the LCO which is found lower than the right coronary ostium (RCO). On this basis, the LCO was chosen to demonstrate the changes associated with AVR. The gross anatomical features of the aortic root were similar to the currently accepted descriptions in textbooks (Townsend *et al*., 2004; Snell, 2008; Standring *et al*, 2008). A total of 60 hearts specimens were divided into 2 Groups of 30 hearts viz. (1) Group A, for the investigation of the aortic root morphometry and; (2) Group B, for the experimental study for evaluation of aortic root changes after placing an oversized prosthesis to simulate AVR in a narrow aortic root.

5.2 GROUP A: AORTIC ROOT DIAMETERS

5.2.1 SAMPLE DEMOGRAPHICS

The aortic root has been extensively studied over the years given that aortic valve surgery has become one of the common operations on the heart. This study was designed to investigate the morphometry of the aortic root and the LCO. Group A was composed 30 hearts viz. 19 males and 11 females. The racial demographics were as follows: 19 Black Indigenous, 7 Indian and 4 White, South Africans. The mean age was 49.7 years (range 23-90 years).

5.2.2 AORTIC ROOT DIAMETERS

The mean aortic annulus diameter in the study group (n=30) was 20.3 mm. This was similar to the diameter of the aortic annulus reported by Tamas and Nylander (2007), Zhu and Zhao (2011) and Son *et al*. (2013) who reported 21.0 mm, 20.4 mm and 23.3 mm, respectively. Vritz *et al*. (2013) and Davis *et al*. (2014) reported aortic annulus diameters of 21 mm and 23.9 mm in males, respectively and 18.7 mm and 20.6 mm in females, respectively. The mean annulus diameter in this current study (20.3 mm) compared favourably with the weighted mean in the reviewed literature (20.7 mm) (Table 6).

The mean diameter at the sino-tubular junction was 21.8 mm. The mean diameter recorded in the present study was similar with the 23.5 mm and 21.6 mm cited by Zhu and Zhao (2011) and Davis *et al* (2014), respectively. However, the mean diameter was smaller than the one recorded as 27 mm(Tamas and Nylander, 2007), 26.1 mm (Son *et al*., 2013) and 26.9 mm and 24.4 mm for males and females respectively as reported by Vritz *et al*., (2013) (Table 6). It should be noted that, the aortic root diameters reported by the authors cited in their studies were measured in live subjects using echocardiography at the end of diastole.

5.2.3 THE AORTIC ROOT DIAMETERS IN RELATION TO SEX

Biaggi *et al*. (2009), Vriz *et al*. (2013) and Davies *et al.* (2014) reported that males were associated with a significantly larger aortic root diameter at the aortic annulus viz. 32 mm *vs* 30 mm, 21 mm *vs* 18.7 mm and 23.9 mm *vs* 20.6 mm, respectively. Vriz *et al*. (2013) and

Davies *et al.* (2014) also reported that males had larger sino-tubular junction diameters than females viz. 26.9 mm *vs* 24.4 mm and 24.4 mm *vs* 21.6 mm, respectively (Table 6).
In the current study, the mean diameter at the aortic annulus in males was slightly larger than in females (20.2 mm *vs* 20.1 mm) (Table 10). The mean diameter at the sino-tubular junction was also slightly larger in males than in females (21.8 mm *vs* 21.6 mm) (Table 10). However, there was no statistically significant difference between the aortic root diameters in males and females. Therefore, in the present study sex was not a major determinant of aortic root diameter. This corroborated the findings of Tamas and Nylander, (2007) who reported that sex was an independent factor in the diameter of the aortic root.

However, studies by Vritz *et al*. (2012) and Zhu and Zhao (2012) showed that when aortic root diameters were indexed to BSA there was no significant difference between males and females. They concluded that the difference in BSA between sexes was responsible for the subsequent difference in aortic root diameters. The above mentioned authors reported that BSA was more useful in predicting the size of the aortic root, hence its use by cardio-thoracic surgeons to determine the size of prosthesis in AVR.

5.2.4 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO RACE

In a study that compared the size of aortic roots in White, African and Latin American groups, Teixido-Tura *et al*. (2015) reported that white males had significantly larger aortic roots than African and Latin American males. The mean aortic annulus diameter was 20.4 mm, 19.6 mm and 21.0 mm in Blacks (n=19), Indians (n=7) and Whites (n=4), respectively (Table 11). The mean sino-tubular junction diameter was 22.0 mm, 21.0 mm and 22.3 mm in Black Indigenous (n=19), Indian (n=7) and White, South Africans (n=4), respectively (Table 11). There was no statistically significant difference in the diameter at the aortic annulus and at the sino-tubular junction among different racial groups. The mean aortic root diameters recorded in the Whites was slightly larger than in Blacks and Indians although this was statistically insignificant.

5.2.5 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO HEIGHT

The present study showed no correlation between the diameter of the aortic root at the annulus and sino-tubular junction and height (p = 0.859) (Table 12). This confirms the findings by Tamas and Nylander (2007) who reported that the height of an individual was an independent factor in the size of the aortic annulus. However, the results of the current study differed from the findings of Vasan *et al*. (1995), Biaggi *et al*. (2009), Zhu and Zhao (2011), Vriz *et al*. (2013), Devereux *et al*. (2012), Wang *et al*. (2012), and Son *et al*. (2013) who all reported that height was a major determinant of the aortic annulus diameter.

5.2.6 THE DIAMETERS OF THE AORTIC ROOT IN RELATION TO AGE

O'Rourke and Nichols (2005) reported that arterial walls stiffen with age and the aortic root and the thoracic aorta dilates with age. The fact that the aortic root diameter increases with age has also been shown clearly in children by Nirdoff *et al*. (1992). In this current study, age had a significant correlation with aortic root diameters viz. aortic annulus (p value = 0.03) and sino-tubular junction (p value = 0.01) (Table 13). The diameter of the aortic annulus and sino-tubular junction increased with age. The finding corroborated the results by Vasan *et al*. (1999), Biaggi *et al*. (2009), Devereux *et al*. (2012), Vriz *et al*. (2012), Zhu and Zhao (2012), Son *et al*. (2013) and Wang *et al*. (2013) who all reported that the diameter of the aortic root increased significantly with age.

5.2.7 THE RELATIONSHIP BETWEEN DIAMETER AT THE AORTIC ANNULUS AND SINO-TUBULAR JUNCTION

The observed aortic annulus diameters and diameter of the aortic root at the sino-tubular junction showed a significant correlation (Figure 28). The diameter of the aortic annulus was approximately 93% that of the sino-tubular junction. The relationship observed was comparable to the reported ratio of 85-90% by Kunzelman *et al.* (1994) and 80-100% by Marom *et al*. (2012). The observed relationship between aortic annulus and sino-tubular junction was slightly different from that observed by Zhu and Zhao (2012), who concluded that the aortic annulus diameter averaged 70% of corresponding sino-tubular junction.

5.3 THE LEFT CORONARY OSTIUM

The shape, position and size of the left coronary ostia was analysed in 30 heart specimens.

5.3.1 SHAPE OF THE LCO

For the hearts analysed, the majority (96.7%) of LCO were circular whilst 3.3% were ellipsoid. A crescenteric LCO was not observed. A Turkish study by Govsa *et al*. (2010) revealed also a majority of LCO that were circular (52%), followed by ellipsoidal (35%) and lastly crescenteric (13%) (Govsa *et al*., 2010).

The findings from the current study differed the results published by Kulkarni and Paranjpe (2014), who reported that 23% of the LCO were circular, 73.3% were horizontally oval 10% were vertically oval.

5.3.2 POSITION OF THE LCO

In the present study the LCO was located below the sino-tubular junction in the majority (73.3%) of the cases. The LCO were also situated on the sino-tubular junction in 23.3% of specimens and above the sino-tubular junction in 3.3% of specimens. In summary, the LCO was located in the left coronary sinus below the sino-tubular junction in the majority of the cases. The findings of the study compared favourably with the results of Govsa *et al*., (2010), Joshi *et al.* (2010) and Kaur *et al.* (2011) who reported that the majority of LCO was located below the sino-tubular junction in 58%, 80% and 78%, respectively (Table 2). The proportion of the LCO located below the sinotubular was higher than the weighted mean (51%) of the reviewed literature (Table 2).

However, Calvacanti *et al.* (2003), Sirikonda and Sreelatha (2012 reported that the LCO were located above and below the sino-tubular junction with equal frequencies. In addition, the findings of the current study did not corroborate the results published by Pedjkovic *et al.* (2008), which illustrated that the majority of LCO were located above the sino-tubular junction (Table 2).

5.3.3 THE HEIGHT OF THE LCO

The distance of the LCO from the aortic annulus is often used to locate the LCO. In the present study, the mean distance was 12.8 mm. The mean distance was slightly greater in males (13.2 mm) than females (11.6 mm) and the difference was not statistically significant

(Table 15). Calvacanti *et al*. (2003), Knight *et al*. (2008), Akhtar *et al*. (2009), Joshi *et al.* (2010) and Ribeiro *et al.* (2013) reported mean distances of the LCO from the aortic annulus of 12.6 mm, 16.0 mm, 15.6 mm, 13.3 mm and 10.3 mm, respectively (Table 19). The mean distance (12.8) of the LCO in the current study compared favourably with the weighted mean of 12.6 mm calculated from the reviewed literature.

Table 19*: Comparison of the LCO height from the aortic annulus with the current study.*

Author (year)	**Sample size (n=)**	**Height of LCO from aortic annulus (mm)**
Calvacanti *et al.* (2003)	51	12.6
Knight *et al.* (2003)	75	16.0
Akhtar *et al.* (2009)	25	15.6
Joshi *et al.* (2010)	103	13.3
Ribeiro *et al.* (2013)	24	10.3
Weighted mean		**12.8**
Current study	**30**	**12.6**

5.3.4 THE DIAMETER OF LCO

The mean diameter of the LCO was 6.1 mm in all the hearts (n=30). The mean diameter in the current study was higher than the diameter recorded by Calvacanti *et al*. (2003), Pejkovic *et al*. (2008), Govsa *et al*. (2010) and Kaur *et al*. (2012) who reported 4.75 mm, 4.1 mm, 4.22 mm and 4.6 mm, respectively (Table 20). The mean diameter of the LCO was also higher than the weighted mean calculated from the reviewed literature (6.1 mm *vs* 4.3 mm).

Calvacanti *et al*. (2003), Pejkovic *et al*. (2008), Govsa *et al*. (2010) and Kaur *et al*. (2012) all analysed formalin fixed heart specimens in their studies. In contrast, in the current study, 'fresh' post mortem specimens that were not embalmed. Clark *et al.* (2014) reported that formalin fixation caused significant shrinkage of tissue samples.

Table 20: *Comparison of the LCO diameters by different authors with the current study.*

Author (year)	**Sample size (n)**	**LCO diameter (mm)**	**Country**
Calvacanti *et al.* (2003)	51	4.75	Brazil
Pejkovic *et al.* (2008)	150	4.1	Austria
Govsa *et al.* (2010)	100	4.22	Turkey
Kaur *et al.*(2012)	77	4.6	India
Weighted mean		**4.3**	
Current study	**30**	**6.1**	**South Africa**

Paulsen *et al*. (1975) stated that the cross-sectional area of the RCO was significantly larger in males than in females. However, in the same series, they found no significant difference in the cross-sectional area of the LCO between males and females. In the current study, the diameter in females was smaller than in males (5.7 *vs* 6.4 mm) although the difference was not statistically significant. The results differed from the findings from Sahni and Jit (1989) and Ilayperuma *et al.* (2011), who showed that mean diameter of the left coronary artery was significantly larger in males than in females.

Sahni and Jit (1989) reported that the diameter of coronary arteries increased significantly with increasing age. However, in this study, there was no significant correlation demonstrated that the size of the coronary arteries increased with an increase in age (Table 16).

The size of the arteries have been shown to differ in different races. For example, Lachman *et al*. (2000) reported that the diameter of the internal thoracic artery of South African Indians was significantly smaller than that of White South Africans. However, in the current study, no significant difference was noted in the diameter of the LCO among Black Indigenous, Indian and White South Africans. There was statistically significant correlation between the diameter of the LCO and height of the individuals (Table 16). Taller individuals had larger diameters of the LCO than their shorter counterparts.

5.4 GROUP B: AORTIC VALVE REPLACEMENT

The objective of this study group was to investigate and document the anatomical changes that resulted from forcing or shoe-horning of an oversized prosthesis into a narrow aortic root during AVR. The study focused primarily on the anatomic changes on the morphology and morphometry of the LCO which may have a catastrophic impact on cardiac function. This was achieved by designing and implementing an experimental model that involved implanting an oversized prosthesis in a normal aortic root to simulate AVR in a narrow aortic root.

5.4.1 CHANGES IN SHAPE OF THE LCO

The LCO is normally situated with the left coronary sinus below the sino-tubular junction (Standring *et al.,* 2008). *Govsa et al.* (2008) described three basic shapes of LCO viz. circular, ellipsoidal and crescentic. Changes in coronary ostial morphology has been noted as a cause of coronary artery obstruction following AVR. Pillai *et al*. (2004) reported that coronary blood flow blockage as an acute complication of AVR may be caused by an oedematous reaction of the ostial wall and spasm of the coronary arteries. Ueda (2010) and Choi *et al*. (2013) reported that distortion of the aortic root anatomy including the coronary ostia can be caused by suturing the aortic valve prosthesis following the wave form of the valve leaflet attachment. In addition, tying down sutures at the commissures first during AVR pulls the aortic annulus upwards, distorting and deforming the coronary ostia. The present study reports changes in the shape of the LCO from circular to the elongated ellipsoidal shape with almost complete obliteration of the orifice. After the insertion of the prosthesis, the vertical diameter of the LCO was reduced significantly while the horizontal diameter increased significantly to almost a slit like shape (Plate 12).

5.4.2 CHANGES IN THE DIAMETER OF THE LCO

To confirm the significant change in the shapes of the LCO, the change in diameters of the LCO was recorded and analysed. In the present study, the mean horizontal and vertical diameters before prosthesis implantation was 4.8 mm. Given the change in shape after implantation of the prosthesis and placing sutures at the co mmissures and following the scalloping attachment of the valve leaflet, analysis of diameters showed significant change in morphometry of the LCO. The findings compare favourably with the reports by Ueda (2010) and Choi *et al*., (2013) who reported that distortions can be produced by suturing techniques.

5.4.3 CHANGES IN THE HEIGHT OF THE LCO

The current study cohort recorded an average LCO height of 10.9 mm from the aortic annulus. The height of the LCO from the aortic annulus changed significantly after an oversized prosthesis was sutured along the attachment of the valve leaflets. The LCO was displaced towards the valve prosthesis by up to 50% of its normal height. The finding concurs with Ribeiro and colleagues (2013), who reported a reduction of 2 mm to 5 mm in height of the LCO from the aortic annulus in patients who had undergone TAVI. From their review of 24 published cases of coronary obstruction, a distance of ≤10 mm of the LCO from the aortic annulus was identified as a risk factor for coronary obstruction (Ribeiro *et al.,* 2013).

5.4.4 RIDGE FORMATION ABOVE THE LCO

Placing an oversized prosthesis resulted in the formation of a ridge in the aorta just above and almost burying the LCO. The ridge extended from the co mmissures adjacent to the LCO and almost burying the LCO (Plate 12). This ridge was created by lateral distraction of the co mmissures, and may also contribute to the distortion and obliteration of the LCO. There is paucity in the available literature concerning the aforementioned changes.

5.5 PLIABILITY OF THE AORTIC ANNULUS AND SINO-TUBULAR JUNCTION

The present study showed that the sino-tubular junction is more pliable than the aortic annulus by a factor of 1.5. The aortic annulus is closely related to the fibro-skeleton of the heart as opposed the aortic sinuses whose walls are like aortic walls (Anderson *et al.*, 2007). The amount of elastic fibres increases as the amount of fibrous material decreases within the wall of the aortic root from the left ventricle to the aorta. Standring *et al* (2008) noted that during systole, when blood is ejected from the left ventricle into the aorta, the sino-tubular diameter increases by 16% whilst at the aortic annulus the diameter does not change.

The afore-mentioned difference may explain the fact that the sino-tubular junction is relatively more pliable than the aortic annulus and this may tempt the unwary surgeon to insert a larger valve than the root can acco mmodate without distortion. Aortic stenosis may be associated with a post-stenotic dilation of the aorta (Whilton and Jahangahiri, 2006), and this appearance creates a false impression of a big root.

CHAPTER 6

CONCLUSION

6.1 SAMPLE DISTRIBUTION

The gross anatomical features of the aortic root in this study corroborated with the description of the aortic root in standard textbooks (Townsend *et al*., 2004; Standring *et al*., 2008). A total of 60 normal post mortem hearts were used for this study.

6.2 AORTIC ROOT DIAMETERS

The mean aortic root diameters at the aortic annulus and sino-tubular junction recorded in this study were 20.2 mm and 21.8 mm respectively. This result confirmed that the aortic root diameter at the sino-tubular junction is larger than that at the aortic annulus. Age was noted to be a strong determinant in the size of the aortic root, confirming earlier reports that the aortic root size increases with age. The size of the aortic root in White males was significantly larger than in black Indigenous South African males, however no significant differences in Indians were noted. Height, sex and race were not determinants of aortic root sizes.

6.3 THE LEFT CORONARY OSTIUM

The shape of the LCO was described according to Govsa *et al*. (2010) as circular, ellipsoidal or crescenteric. In the current study, the majority of LCO was circular (96.3%) followed by ellipsoidal (3.3%). None of the LCO had a crescenteric shape.

The study concluded that the majority of LCO are located below the sino-tubular junction. The mean height of the LCO from the aortic annulus was 12.6 mm. The present study concluded that sex, race, height and age did not significantly affect the distance of the LCO from the aortic annulus.

The mean diameter of the LCO was recorded at 6.1 mm. The study concluded that males have a larger LCO than females although this was not statistically not significant. The study also concluded that height of an individual has a positive correlation with the diameter of the LCO. However age and race did not significantly affect the size of the LCO.

6.4 AORTIC VALVE REPLACEMENT

The objective of this experimental study was to investigate and document the anatomical changes in the aortic root that may result from forcing or shoe-horning an oversized prosthesis into a narrow aortic root during AVR. The study focused on the anatomic changes on the morphology and morphometry of the LCO which may have catastrophic impact on cardiac function.

The following anatomical observation were made with regard to AVR, where the valve was oversized in relation to the valve annulus.

1. Inserting an oversized valve caused the following effects:
   (a) The left coronary orifice was markedly distorted, even to the point of obliteration
   (b) A transverse ridge of aortic tissue, in the form of a tight bar was created above the LCO.
   (c) There was caudal displacement of the LCO towards the valve prosthesis.

This study clearly shows the pitfalls in oversizing an Aortic Valve prosthesis, during valve replacement. The anatomic sequelae of forcibly inserting an oversized prosthesis have been clearly demonstrated.

6.5 PLIABILITY OF THE AORTIC ANNULUS AND SINO-TUBULAR JUNCTION

The sino-tubular junction is relatively more pliable in comparison to the valve annulus being part of the fibrous skeleton of the heart. The sino-tubular junction is more elastic. This allows placement of a valvular prosthesis considerably bigger than the size of the annulus in the supra-annular position. The sino-tubular junction is more pliable than the annulus by a factor of 1.5.

6.6 STUDY LIMITATIONS

The limitations of the present study were: the absence of body weight because the body scale was not available at the State Mortuary. Thus the BSA could not be calculated. The study to investigate the normal morphometry was conducted on post mortem hearts, while relatively accurate, live patients would have provided a better and more representative functional anatomy. Heart specimens used in the experiment had a normal aortic root instead of a narrow aortic root so there was deliberate use of oversized prostheses and sizers.

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APPENDIX

Results: Shape, size and position of the left coronary ostia. 30 fresh hearts

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
1	Black	Female	oval	below	10.0	4.5
					10.5	5.0
					11.0	5.0
AVG					10.5	4.8
2	White	Male	oval	below	12.0	8.5
					13.5	7.5
					13.0	8.0
AVG					12.8	8.0
3	Black	Male	oval	on	12.0	5.5
					13.0	5.0
					11.0	6.5
AVG					12.0	5.7
4	Indian	Female	oval	below	11.0	4.0
					12.0	4.5
					11.0	5.0
AVG					11.3	4.5
5	Black African	Female	oval	below	12.0	6.5
					11.5	5.5
					12.0	6.0
AVG					11.8	6.0

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
6	Black	Male	oval	on	16.0	6.0
					15.5	7.0
					15.5	7.0
AVG					15.7	6.7
7	Black	Male	oval	below	15.5	4.0
					15.0	5.0
					15.0	6.0
AVG					15.2	5.0
8	Black	Female	oval	below	13.0	6.0
					11.5	5.5
					12.0	7.0
AVG					12.2	6.2
9	Black	Female	oval	below	12.0	5.0
					13.0	6.0
					13.0	6.0
AVG					12.7	5.7
10	Black	Female	oval	below	11.0	5.5
					12.0	5.5
					12.0	6.0
AVG					11.7	5.7

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
11	Black	Male	oval	below	10.0	4.5
					11.0	4.5
					10.5	5.0
AVG					10.5	4.7
12	Black	Male	oval	below	14.0	5.0
					13.0	5.5
					14.0	5.0
AVG					13.7	5.2
13	White	Male	oval	below	12.0	5.5
					11.5	6.5
					12.0	5.5
AVG					11.8	5.8
14	Black	Female	oval	below	11.0	6.0
					11.0	6.5
					11.5	7.0
AVG					11.2	6.5
15	Indian	Female	oval	below	10.5	3.5
					10.0	4.5
					11.0	4.5
AVG					10.5	4.2

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
16	White	Male	oval	on	14.5	4.5
					13.0	5.5
					14.0	5.0
AVG					13.8	5.0
17	Black	Female	oval	on	13.5	4.5
					12.5	5.5
					14.0	5.0
AVG					13.3	5.0
18	Black	Male	oval	on	12.0	8.0
					11.5	8.0
					12.0	9.0
AVG					11.8	8.3
19	Indian	Female	oval	below	15.5	5.5
					16.0	6.0
					16.0	6,0
AVG					15.8	5.8
20	Black	Male	oval	below	15.0	6.0
					16.0	7.0
					15.5	7.5
AVG					15.5	6.8

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
21	White	Male	oval	below	15.0	6.5
					15.0	6.5
					16.0	7.0
AVG					15.3	6.7
22	Indian	Female	oval	below	16.0	5.0
					14.5	4.5
					15.0	4.5
AVG					15.2	4.7
23	Indian	Male	oval	on	13.5	7.5
					14.0	6.5
					13.0	7.0
AVG					13.5	7.0
24	Indian	Male	ellipsoid	on	11.5	9.5
					12.0	8.5
					10.5	8.5
AVG					11.3	8.8
25	Indian	Male	oval	below	9.0	5.0
					10.0	6.0
					10.0	6.0
AVG					9.7	5.7

Specimen	Race	Sex	Shape of LCO	Position of LCO with reference to STJ	Height of LO from aortic annulus	LCO diameter
26	Black	Male	oval	below	11.5	6.0
					11.0	7.0
					12.0	5.5
AVG					11.5	6.2
27	Black	Male	oval	below	11.5	4.5
					12.5	5.5
					11.5	6.0
AVG					11.8	5.3
28	Indian	Male	oval	below	12.5	8.0
					12.0	9.0
					12.0	8.5
AVG					12.2	8.5
29	Black	Male	oval	Above 3mm	18,5	9.0
					17.5	7.5
					18.0	8.0
AVG					18.0	8.2
30	Black	Male	oval	below	13.5	5.0
					13.0	4.0
					13.5	6.0
AVG					13.3	5.0

Results: Race, sex, height, Age, LCO position and mean LCO diameters

Sample number	Race	Sex	Age (years)	Body height (cm)	LCO shape	Position of LCO with reference to STJ	Mean height of LCO from aortic annulus	LCO diameter
1	Black	Female	33	171	Circular	Below	10.5	4.8
2	White	Male	55	178	Circular	Below	12.8	8.0
3	Black	Male	25	168	Circular	Below	12.0	5.7
4	Indian	Female	29	162	Circular	Below	11.3	4.5
5	Black	Female	41	171	Circular	Below	11.8	6.0
6	Black	Male	35	168	Circular	On	15.7	6.7
7	Black	Male	29	165	Circular	Below	15.2	5.0
8	Black	Female	32	178	Circular	Below	12.2	6.2
9	Black	Female	41	162	Circular	Below	12.7	5.7
10	Black	Female	58	183	Circular	Below	11.7	5.7
11	Black	Male	23	164	Circular	Below	10.5	4.7
12	Black	Male	46	165	Circular	Below	13.7	5.2
13	White	Male	34	183	Circular	Below	11.8	5.8
14	Black	Female	63	169	Circular	Below	11.2	6.5
15	Indian	Female	78	151	Circular	Below	10.5	4.2
16	White	Male	77	180	Circular	On	13.8	5.0
17	Black	Female	45	175	Circular	On	13.3	5.0
18	Black	Male	38	171	Circular	On	11.8	8.3
19	Indian	Female	82	151	Circular	Below	15.8	5.8
20	Black	Male	90	163	Circular	Below	15.5	6.8
21	White	Male	72	170	Circular	Below	15.3	6.7
22	Indian	Female	58	165	Circular	Below	15.2	4.7
23	Indian	Male	25	170	Circular	On	13.5	7.0
24	Indian	Male	40	165	Ellipsoid	On	11.3	8.8

25	Indian	Male	68	167	Circular	Below	9.7	5.7
26	Black	Male	42	152	Circular	Below	11.5	6.2
27	Black	Male	34	153	Circular	Below	11.8	5.3
28	Indian	Male	68	180	Circular	Below	12.2	8.5
29	Black	Male	38	182	Circular	Above 3mm	18.0	8.2
30	Black	Male	38	169	Circular	Below	13.3	5.0

Results aortic root and aortic sinus dimensions

Sample number	Race	Age (years)	Height (cm)	Sex	Aortic annulus diameter (mm)	Diameter at the STJ (mm)
1	Black	33	171	Female	19.0	20.5
					19.0	21.0
					18.5	21.0
AVG					18.8	20.8
2	White	55	178	Male	22.5	23.0
					22	24.0
					22.5	23.0
AVG					22.3	23.3
3	Black	25	168	Male	17,5	19.0
					18.0	19.5
					18.5	20.0
AVG					18.5	19.5
4	Indian	29	162	Female	18.5	19.5
					19.0	20.0
					18.0	19.5
AVG					18.5	19.7
5	Black	41	171	Female	22.5	24.5
					23.5	25.0
					24.0	25.0
AVG					23.3	24.8

Sample number	Race	Age (years)	Height /cm	Sex	Aortic annulus diameter (mm)	Diameter at the STJ (mm)
6	Black	35	168	Male	18.0	18.5
					17.0	19.0
					18.0	19.5
AVG					17.6	19.0
7	Black	29	165	Male	18.0	18.5
					17.0	20.0
					18.0	19.0
AVG					17.7	19.2
8	Black	32	178	Female	19.0	20.0
					18.0	21.0
					19.0	21.0
AVG					18.7	20.7
9	Black	41	162	Female	22.0	22.5
					21.5	23.0
					22.0	23.0
AVG					21.8	22.8
10	Black	58	183	Female	22.0	23.0
					22.0	23.0
					21.5	23.0
AVG					21.8	23

Sample number	**Race**	**Age (years)**	**Height (cm)**	**Sex**	**Aortic annulus diameter (mm)**	**Diameter at Sino-tubular junction (mm)**
11	Black	23	164	Male	21.0	21.0
					20.0	21.0
					19.0	20.5
AVG					19,7	20.8
12	Black	46	165	Male	18.5	19.0
					18.0	19.5
					19.0	20.5
AVG					18.5	19.7
13	White	34	183	Male	19.5	20.5
					19.0	20.5
					19.5	21.0
AVG					19.3	20.7
14	Black	63	169	Female	20.0	21,5
					21.0	22.0
					20.0	21.5
AVG					20.3	21,7
15	Indian	78	151	Female	17.0	18.0
					17.0	17.5
					17.0	18.0
AVG					17.0	17.8

Sample number	Race	Age (years)	Height (cm)	Sex	Aortic annulus diameter (mm)	Diameter at Sino-tubular junction (mm)
16	White	77	180	Male	20.5	21.5
					20.0	21.5
					21.5	22.5
AVG					20.7	21.8
17	Black	45	175	Female	20.0	21.5
					19.5	21.0
					19.0	21.5
AVG					19.5	21.3
18	Black	38	171	Male	20.0	21.0
					21.0	21.5
					20.0	22.0
AVG					20.3	21.5
19	Indian	82	151	Female	19.5	22.0
					19.0	22.0
					19.0	21.5
AVG					19.2	21.8
20	Black	90	163	Male	23.0	26.5
					23.0	26.0
					24.0	27.0
AVG					23.3	26.5

Sample number	Race	Age (years)	Height (cm)	Sex	Aortic annulus diameter (mm)	Diameter at Sino-tubular junction (mm)
21	White	72	170	Male	21.5	23.5
					21.0	23.0
					22.0	23.5
AVG					21.5	23.3
22	Indian	58	165	Female	21.5	22.5
					21.0	23.0
					22.5	23.0
AVG					21.6	22.8
23	Indian	25	170	Male	16.0	18.0
					16.0	18.0
					15.0	18.5
AVG					15.7	18.2
24	Indian	40	165	Male	18.5	19.0
					18.0	20.0
					19.0	21.0
AVG					18.5	20
25	Indian	68	167	Male	23.5	25.5
					24.0	26.0
					24.0	26.0
AVG					23.8	25.8

Sample number	Race	Age (years)	Height (cm)	Sex	Aortic annulus diameter (mm)	Diameter at Sino-tubular junction (mm)
26	Black	42	152	Male	22.5	25.0
					23.0	26.0
					22.5	25.5
AVG					22.7	25.5
27	Black	34	153	Male	19.0	21.0
					19.5	20.5
					19.0	20.0
AVG					19.2	20.5
28	Indian	68	180	Male	24.0	26.5
					24.0	27.0
					23.5	26.0
AVG					23.8	26.5
29	Black	38	182	Male	21.5	22.5
					21.0	23.0
					21.0	23.0
AVG					21.2	22.8
30	Black	38	169	Male	20.5	21.5
					21.0	22.0
					20.0	21.5
AVG					20.5	21.7

Results: Age, sex, race, height and mean aortic root diameters

Sample number	Race	Sex	Age (years)	Body height (cm)	Mean aortic annulus diameter (mm)	Mean sino-tubular junction Diameter at (mm)
1	Black	Female	33	171	18.8	20.8
2	White	Male	55	178	22.3	23.3
3	Black	Male	25	168	18.5	19.5
4	Indian	Female	29	162	18.5	19.7
5	Black	Female	41	171	23.3	24.8
6	Black	Male	35	168	17.6	19.0
7	Black	Male	29	165	17.7	19.2
8	Black	Female	32	178	18.7	20.7
9	Black	Female	41	162	21.8	22.8
10	Black	Female	58	183	21.8	23
11	Black	Male	23	164	19.7	20.8
12	Black	Male	46	165	18.5	19.7
13	White	Male	34	183	19.3	20.7
14	Black	Female	63	169	20.3	21.7
15	Indian	Female	78	151	17.0	17.8
16	White	Male	77	180	20.7	21.8
17	Black	Female	45	175	19.5	21.3
18	Black	Male	38	171	20.3	21.5
19	Indian	Female	82	151	19.2	21.8
20	Black	Male	90	163	23.3	26.5
21	White	Male	72	170	21.5	23.3
22	Indian	Female	58	165	21.6	22.8
23	Indian	Male	25	170	15.7	18.2
24	Indian	Male	40	165	18.5	20
25	Indian	Male	68	167	23.8	25.8

26	Black	Male	42	152	22.7	25.5
27	Black	Male	34	153	19.2	20.5
28	Indian	Male	68	180	23.8	26.5
29	Black	Male	38	182	21.2	22.8
30	Black	Male	38	169	20.5	21.7

Averages: Changes in the aortic root after implantation of prosthesis

Results: Changes in the aortic root after implantation of prosthesis

Before Insertion Of Prosthesis					Size Of Prosthesis Inserted	After Insertion Of Prosthesis				
Specimen No	Annular Size	Shape Of LCO	Diameter Of LCO V/H	Height Of LCO From Annulus		Shape Of LCO	Diameter Of LCO V/H		Height Of LCO From Annulus	Distortion Of The Aortic Wall Formed (Y/N)
1	23	Circular	5.5	7.0	27	Ellipsoid	2	9.0	2.5	Y
			6.0	8.0			1.5	8.5	3.5	
			5.5	8.0			1.5	8.0	2.5	
AVG			5.7	7.7			1.7	8.5	2.8	
2	23	Circular	6.5	10.5	27	Ellipsoid	2.5	8.5	3.5	Y
			4.5	9.5			2.5	7.5	4.5	
			6.0	9.5			2	9.0	3.0	
AVG			5.7	9.8			2.3	8.3	3.7	
3	23	Circular	4.5	11.0	27	Ellipsoid	1.0	6.5	6.0	Y
			4.0	11.0			1.0	7.5	5.0	
			4.0	10.5			1.0	7.0	5.0	
AVG			4.2	10.8			1.0	7.0	5.3	
4	19	Circular	6.5	13.0	23	Ellipsoid	1.5	9.5	8.0	Y
			6.0	14.0			1.0	8.5	7.0	
			6.0	12.5			2.0	8.5	6.5	
AVG			6.2	9.3			1.5	8.8	7.2	

KEY LCO – Left Coronary Ostium; STJ – Sinotubular Junction; V – Vertical; H - Horizontal

Averages: Changes in the aortic root after implantation of prosthesis

Before Insertion Of Prosthesis					Size Of Prosthesis Inserted	After Insertion Of Prosthesis				
Specimen No	Annular Size	Shape Of LCO	Diameter Of LCO V/H	Height Of LCO From Annulus		Shape Of LCO	Diameter Of LCO V/H		Height Of LCO From Annulus	Distortion Of The Aortic Wall Formed (Y/N)
5	21	Circular	4.0	10.0	25	Ellipsoid	1.5	7.5	4.0	Y
			5.0	9.5			1.0	8.0	5.0	
			4.0	11.0			1.0	7.0	5.5	
AVG			4.3	10.2			1.2	7.5	4.8	
6	21	Circular	6.0	10.0	25	Ellipsoid	2.0	8.5	4.5	Y
			6.0	9.0			1.5	8.0	4	
			6.5	9.0			1.5	7.5	4	
AVG			6.2	9.3			1.7	8.0	4.2	
7	19	Circular	6.0	13.0	23	Ellipsoid	1.5	9.0	6.5	Y
			5.0	12.0			1.5	9.0	6.0	
			5.5	12.0			2.0	10.0	5.5	
AVG			5.5	12.3			1.7	9.3	6.0	
8	19	Circular	5.5	12.0	23	Ellipsoid	2.5	8.0	5.5	Y
			5.0	11.0			1.5	9.0	5.0	
			5.0	11.5			1.5	9.5	5.0	
AVG			5.2	11.5			1.8	8.8	5.2	
9	19	Circular	5.5	10	23	Ellipsoid	1.5	8.0	5.0	Y
			5.5	10.5			2.0	7.5	5.5	
			6.0	11.5			1.5	8.5	5.5	
AVG			5.7	10.7			1.7	8.0	5.3	

Averages: Changes in the aortic root after implantation of prosthesis

Before Insertion Of Prosthesis					Size Of Prosthesis Inserted	After Insertion Of Prosthesis				
Specimen No	Annular Size	Shape Of LCO	Diameter Of LCO V/H	Height Of LCO From Annulus		Shape Of LCO	Diameter Of LCO V/H		Height Of LCO From Annulus	Distortion Of The Aortic Wall Formed (Y/N)
10	19	Circular	5.0	11.0	23	Ellipsoid	2.0	7.5	4.0	Y
			4.5	12.0			1.5	8.0	4.5	
			4.5	12.5			2.0	9.0	4.5	
AVG			4.7	11.8			1.8	8.2	4.3	
11	21	Circular	5.0	10.5	25	Ellipsoid	1.5	8.5	7.0	Y
			4.5	11.5			2.5	7.0	6.0	
			5.5	10.0			1.5	7.5	6.0	
AVG			5.0	10.7			1.8	7.7	6.3	
12	21	Circular	4.5	11.0	25	Ellipsoid	1.5	7.5	6.5	Y
			4.0	12.0			1.5	8.5	5.5	
			5.0	12.0			1.0	8.5	5.5	
AVG			4.5	11.7			1.3	8.2	5.8	
13	19	Circular	4.0	13.0	23	Ellipsoid	1.0	7.5	7.5	Y
			5.0	12.5			1.0	8.0	6.0	
			4.0	12.5			1.0	8.0	7.0	
AVG			4.3	12.7			1.0	7.8	6.8	

Averages: Changes in the aortic root after implantation of prosthesis

Before Insertion Of Prosthesis						After Insertion Of Prosthesis				
Specimen No	Annular Size	Shape Of LCO	Diameter Of LCO V/H	Height Of LCO From Annulus	Size Of Prosthesis Inserted	Shape Of LCO	Diameter Of LCO V/H		Height Of LCO From Annulus	Distortion Of The Aortic Wall Formed (Y/N)
14	21	Circul	5.0	12.0	25	Ellipsoid	1.5	8.5	8.5	Y
			5.0	13.0			1.5	8.0	7.0	
			5.0	11.5			2.5	9.5	7.0	
AVG			5.0	12.2			1.83	8.7	7.5	
15	21	Circul	6.0	13.0	25	Ellipsoid	2.0	7.5	6.0	Y
			5.0	13.0			1.5	8.5	6.5	
			5.0	12.5			1.5	8.0	7.5	
AVG			5.3	12.8			1.7	8.0	6.7	
16	23	Circle	4.0	13.5	27	Ellipsoid	1.0	10.0	4.0	Y
			4.5	14.5			2.0	8.0	5.0	
			4.5	13.0			1.0	9.5	5.5	
Average			4.3	13.7			1.3	9.2	4.8	
17	19	Circle	3.5	10.0	23	Ellipsoid	2.0	8.0	5.5	Y
			4.5	9.0			2.0	9.0	6.5	
			3.0	10.5			1.5	8.0	6.0	
Average			3.7	9.8			1.7	8.3	6.0	
18	<19	Circle	5.5	15.0	23	Ellipsoid	1.0	8.5	4.5	Y
			4.0	13.5			1.5	9.5	6.0	

Averages: Changes in the aortic root after implantation of prosthesis

			5.5	14.5			2.5	8.0	5.0	
Average			5.0	14.3			1.7	8.7	5.2	
19	23	Circle	4.0	13.0	27	Ellipsoid	2.5	7.0	4.0	Y
			3.5	14.5			2.0	8.0	6.5	
			5.0	14.5			2.0	9.0	5.5	
Average			4.2	14.0			2.2	8.0	5.3	
20	21	Circle	5.0	11.5	25	Ellipsoid	1.5	8.0	5.0	Y
			4.0	10.5			1.0	9.0	4.0	
			4.0	10.5			1.0	7.5	5.5	
Average			4.3	10.8			1.2	8.2	4.8	
21	19	Circle	3.5	12.0	23	Ellipsoid	1.5	6.5	4.5	Y
			3.0	11.0			1.0	6.0	5.5	
			3.5	12.5			1.0	7.0	5.5	
Average			3.3	11.8			1.2	6.5	5.2	
22	23	Circle	5.5	14.0	27	Ellipsoid	2.0	8.5	6.5	Y
			4.5	12.0			2.0	7.5	5.0	
			4.0	12.5			1.5	7.5	6.5	
Average			4.7	12.8			1.8	7.8	6.0	
23	21	Circle	4.0	14.0	25	Ellipsoid	1.5	8.0	4.5	Y
			5.0	14.5			1.5	8.5	4.0	
			5.5	13.5			2.0	9.5	5.5	
Average			4.8	14.0			1.7	8.7	4.6	
24	19	Circle	5.0	13.5	23	Ellipsoid	1.0	8.5	5.0	Y
			4.0	12.5			1.0	9.5	6.0	
			5.5	12.0			2.0	8.0	5.0	
Average			4.8	12.7			1.3	8.7	5.3	

Averages: Changes in the aortic root after implantation of prosthesis

25	21	Circle	3.5	14.0	25	Ellipsoid	1.0	10.0	4.5	Y
			4.5	13.0			2.0	9.0	4.0	
			5.5	13.0			2.0	8.5	4.0	
Average			4.5	13.3			1.7	9.2	4.2	
26	23	Circle	4.5	11.0	27	Ellipsoid	2.0	9.0	3.0	Y
			5.5	10.0			2.5	8.5	4.0	
			5.5	12.0			1.5	7.5	4.5	
Average			5.2	11.0			2.0	8.3	3.8	
27	19	Circle	3.5	15.0	23	Ellipsoid	1.0	8.0	5.0	Y
			4.5	13.5			1.0	7.0	4.0	
			3.0	13.0			1.0	7.0	5.0	
Average			3.7	13.8			1.0	7.3	4.7	
28	19	Circle	5.0	13.0	23	Ellipsoid	1.0	9.5	6.5	Y
			4.0	12.0			2.0	8.5	5.0	
			4.0	13.5			2.5	7.5	5.0	
Average			4.3	12.8			1.8	8.5	5.5	
29	<19	Circle	4.0	10.0	23	Ellipsoid	2.0	8.0	6.5	Y
			5.0	9.0			2.0	7.5	5.5	
			3.5	10.5			1.5	7.5	5.5	
Average			4.2	9.8			1.8	7.7	5.8	
30	23	Circle	6.0	18.0	27	Ellipsoid	2.5	8.5	6.0	Y
			5.0	16.0			2.0	7.0	5.0	
			5.0	17.0			2.0	9.0	5.0	
Average			5.3	17.0			2.2	8.2	5.3	

Averages: Changes in the aortic root after implantation of prosthesis

Before Insertion Of Prosthesis					Size Of Prosthesis Inserted (Mm)	After Insertion Of Prosthesis				
Specimen No	Annular Size	Shape Of LCO	Diameter Of LCO V/H (Mm)	Height Of LCO From Annulus (Mm)		Shape Of LCO	Vertical Diameter Of LCO (Mm)	Horizontal Diameter Of LCO (Mm)	Height Of LCO From Annulus (Mm)	Distortion Of The Aortic Wall Formed (Y/N)
1	23	Circular	5.7	7.7	27	Ellipsoid	1.7	8.5	2.8	Y
2	23	Circular	5.7	9.8	27	Ellipsoid	2.3	8.3	3.7	Y
3	23	Circular	4.2	10.8	27	Ellipsoid	1.0	7.0	5.3	Y
4	19	Circular	6.2	9.3	23	Ellipsoid	1.5	8.8	7.2	Y
5	21	Circular	4.3	10.2	25	Ellipsoid	1.2	7.5	4.8	Y
6	21	Circular	6.2	9.3	25	Ellipsoid	1.7	8.0	4.2	Y
7	19	Circular	5.5	12.3	23	Ellipsoid	1.7	9.3	6.0	Y
8	19	Circular	5.2	11.5	23	Ellipsoid	1.8	8.8	5.2	Y
9	19	Circular	5.7	10.7	23	Ellipsoid	1.7	8.0	5.3	Y
10	19	Circular	4.7	11.8	23	Ellipsoid	1.8	8.2	4.3	Y
11	21	Circular	5.0	10.7	25	Ellipsoid	1.8	7.7	6.3	Y
12	21	Circular	4.5	11.7	25	Ellipsoid	1.3	8.2	5.8	Y
13	19	Circular	4.3	12.7	23	Ellipsoid	1.0	7.8	6.8	Y
14	21	Circular	5.0	12.2	25	Ellipsoid	1.8	8.7	7.5	Y
15	21	Circular	5.3	12.8	25	Ellipsoid	1.7	8.0	6.7	Y
16	23	Circular	4.3	13.7	27	Ellipsoid	1.3	9.2	4.8	Y
17	21	Circular	3.7	9.8	25	Ellipsoid	1.7	8.3	6.0	Y
18	>19	Circular	5.0	14.3	23	Ellipsoid	1.7	8.7	5.2	Y
19	23	Circular	4.2	14.0	27	Ellipsoid	2.2	8.0	5.3	Y
20	21	Circular	4.3	10.8	25	Ellipsoid	1.2	8.2	4.8	Y
21	19	Circular	3.3	11.8	23	Ellipsoid	1.2	6.5	5.2	Y
22	23	Circular	4.7	12.8	27	Ellipsoid	1.8	7.8	6.0	Y
23	21	Circular	4.8	14.0	25	Ellipsoid	1.7	8.7	4.6	Y
24	19	Circular	4.8	12.7	23	Ellipsoid	1.3	8.7	5.3	Y

Averages: Changes in the aortic root after implantation of prosthesis

25	21	Circular	4.5	13.3	25	Ellipsoid	1.7	9.2	4.2	Y
26	23	Circular	5.2	11.0	27	Ellipsoid	2.0	8.3	3.8	Y
27	19	Circular	3.7	13.8	23	Ellipsoid	1.0	7.3	4.7	Y
28	19	Circular	4.3	12.8	23	Ellipsoid	1.8	8.5	5.5	Y
29	<19	Circular	4.2	9.8	23	Ellipsoid	1.8	7.7	5.8	Y
30	23	Circular	5.3	17.0	27	Ellipsoid	2.2	8.2	5.3	Y

PLIABILITY OF THE AORTIC ANNULUS AND THE SINO-TUBULAR JUNCTION

Specimen	Aortic annulus diameter	Maximum stretch	Difference	Sino-tubular junction	Maximum stretch	Difference
1	22.0	36.0		24.5	48.0	
	21.0	35.0		25.0	48.0	
	22.5	37.5		24.0	47.0	
Average	21.8	34.2	12.4	24.5	47.7	23.2
2	18.0	35.5		21.0	44.5	
	19.0	37.0		22.0	45.0	
	18.0	35.0		20.5	44.0	
Average	18.3	35.8	17.5	21.2	44.5	23.3
3	17.0	34.0		20.0	44.0	
	18.0	35.5		21.0	46.0	
	17.0	34.0		19.5	48.0	
Average	17.3	34.5	17.2	20.2	46	25.8
4	24.0	40.0		26.0	56.0	
	24.0	41.0		27.0	59.0	
	22.5	39.5		28.5	56.0	
Average	23.5	40.5	17.0	27.2	56.3	29.1
5	20.0	37.0		23.0	53.0	
	21.0	37.0		22.5	49.0	
	19.5	38.5		23.5	51.5	
Average	20.2	37.5	17.3	23	51.2	28.2

Specimen	Aortic annulus diameter	Maximum stretch	Different	Sino-tubular junction	Maximum stretch	Different
6	19.0	38.5		22.0	50.5	
	20.0	39.0		21.0	48.0	
	20.5	38.0		20.5	47.0	
Average	19.8	38.5	18.7	21.2	48.5	27.3
7	22.5	40.5		23.0	53.0	
	23.0	39.0		22.0	49.0	
	22.0	39.5		23.5	51.5	
Average	22.5	39.5	17.0	22.8	51.2	28.4
8	20.5	39.0		22.5	46.5	
	21.5	38.0		23.5	46.0	
	19.0	38.5		22.0	48.5	
Average	20.3	38.5	18.2	22.7	46.7	24.0
9	18.0	38.5		21.0	46.0	
	19.0	39.5		20.0	48.0	
	18.0	38.0		20.5	49.5	
Average	18.3	38.7	20.4	20.5	47.8	27.3
10	21.5	37.5		23.5	53.0	
	20.5	37.0		25.5	50.5	
	21.0	38.5		24.5	51.5	
Average	21.0	37.7	16.7	23.7	51.7	28.0
11	23.0	44.5		25.5	53.5	
	22.0	44.5		24.0	57.0	
	22.5	43.0		24.0	58.0	
Average	22.5	44.0	21.5	24.2	55.8	31.3

Specimen	Aortic annulus diameter	Maximum stretch	Different	Sino-tubular junction	Maximum stretch	Different
12	19.5	35.0		20.5	45.0	
	18.5	36.5		22.0	47.5	
	20.0	35.0		20.0	48.5	
Average	19.3	35.5	16.2	20.8	47.0	26.2
13	17.0	33.0		18.5	44.0	
	18.5	34.0		19.5	45.0	
	17.0	34.5		18.5	44.0	
Average	17.5	33.8	16.3	18.8	44.3	25.5
14	16.5	37.0		17.5	46.5	
	17.5	38.0		19.0	47.5	
	18.0	37.0		18.0	47.0	
Average	17.3	37.3	20.0	18.2	47.0	28.8
15	24.5	41.0		25.5	52.5	
	24.0	42.5		27.0	56.0	
	23.0	43.5		25.0	56.0	
Average	23.8	42.3	18.5	23.8	54.8	29.0

MEAN CHANGE OF THE AORTIC ANNULUS AND THE SINO-TUBULAR JUNCTION AFTER PLIABILITY TESTS.

Specimen number	Mean aortic annulus diameter	Mean aortic annulus diameter at maximum stretch	Mean difference at the aortic annulus	Sino-tubular junction	Maximum stretch	Mean difference at the sino-tubular
1	21.8	34.2	12.40	24.5	47.7	23.20
2	18.3	35.8	17.50	21.2	44.5	23.30
3	17.3	34.5	17.20	20.2	46.0	25.80
4	23.5	40.5	17.00	27.2	56.3	29.10
5	20.2	37.5	17.30	23	51.2	28.20
6	19.8	38.5	18.70	21.2	48.5	27.30
7	22.5	39.5	17.00	22.8	51.2	28.40
8	20.3	38.5	18.20	22.7	46.7	24.00
9	18.3	38.7	20.40	20.5	47.8	27.30
10	21.0	37.7	16.70	23.7	51.7	28.00
11	22.5	44.0	21.50	24.5	55.8	31.30
12	19.3	35.5	16.20	20.8	47.0	26.20
13	17.5	33.8	16.30	18.8	44.3	25.50
14	17.3	37.3	20.00	18.2	47.0	28.80
15	23.8	42.3	18.50	25.8	54.8	29.00

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Index: 44/09/2015

23rd September 2015

Dr W Mushiwokufa
Department of Clinical Anatomy
School of Laboratory Medicine and Medical Sciences
University of KwaZulu-Natal

Dear Dr Mushiwokufa

GATE KEEPER PERMISSION: BE307/15

Permission is hereby granted for you to have access to hearts (as stipulated in your research protocol) during routine autopsy examinations at the Gale Street Medico-Legal Mortuary.

Permission is granted on the basis that ethical conduct will be maintained and that standard dissection procedures will be followed. Furthermore, no confidential information will be collected during the data collection process for this project. Kindly also note that no post-mortem numbers will be revealed in the study and data will be randomized before statistical analysis

Should you require any further information or have any queries, please do not hesitate to contact me.

Yours sincerely

S M Aiyer
23 September 2015

Dr SM Aiyer
Acting Chief Specialist
Forensic Pathology Services

UNIVERSITY OF KWAZULU-NATAL ™

INYUVESI YAKWAZULU-NATALI

20 October 2015

Mr W Mushiwokufa
Department of Clinical Anatomy
School of Laboratory Medicine and Medical Sciences
wmushiwokufa@yahoo.com

Dear Mr Mushiwokufa

Protocol: Aortic valve replacement: Anatomical considerations in a narrow aortic root.
Degree: MMedSc
BREC reference number: BE307/15

EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 07 July 2015.

The study was provisionally approved pending appropriate responses to queries raised. Your responses dated 09 September 2015 to queries raised on 09 September 2015 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval.

This approval is valid for one year from **20 October 2015.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its meeting taking place on **10 November 2015.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

1 Professor J Tsoka-Gwegweni
Chair: Biomedical Research Ethics Committee

cc supervisor: satyapalk@ukzn.ac.za