Anatomic Study of the Morphologic Relationship between the Proximal Left and Right Coronary Arteries

By

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Submitted in fulfilment of the requirements for the degree of Masters in Medical Science in the School of Laboratory Medicine and Medical Sciences, University of Kwazulu-Natal

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DECLARATION

I, Ms S. Singh, declare that:

(i) The work described in this dissertation has not been previously submitted to UKZN or any other tertiary institution for purposes of obtaining a degree or any other academic qualification, whether by myself or any other party

(ii) The research reported in this dissertation, except where otherwise indicated, is my original work. Together with my supervisor and co-supervisors, I conceptualised the topic, I developed the protocol and the ethics application with the guidance and support of my supervisor, co-supervisors and statistician, conducted the survey and entered the data by myself and together with the statistician and guidance by my supervisor and co-supervisors completed the analysis of the data obtained.

(iii) I drafted the article and together with my supervisor's and co-supervisors' guidance, input and support submitted the article to the journal. I have completed the dissertation with the guidance and support of my supervisor and co-supervisors.

(iv) This dissertation does not contain another person's data, graphs, tables or other information, unless specifically acknowledged as being sourced from other persons.

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LIST OF ACRONYMS

 \mathbf{A} – aorta

- AIB anterior interventricular branch of left coronary artery
- CX circumflex branch of left coronary artery
- MA median artery
- LCA left coronary artery
- PA pulmonary artery
- **PIB** posterior interventricular branch
- **RCA** right coronary artery

POPULATION GROUPING – In relation to this study, the sample population was divided into Black African, White and Indian individuals

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ABSTRACT

Arising from the aorta, the right (RCA) and left (LCA) coronary arteries provide the arterial supply to the heart. An extensive literature review revealed that most studies have either evaluated the morphology of the RCA or the LCA independently. This study aimed to document the relationship between the morphology of the RCA and LCA using coronary angiograms and fetal dissections. In addition, variations such as split or double RCA and absence of the LCA was documented.

A review of 500 coronary angiograms and a fetal dissection of 41 heart specimens was conducted. The RCA and LCA were classified according to their branching patterns and arterial dominance. The embryologic relationship between the RCA and the LCA was also documented including their lengths and diameters.

The angiographic review showed that the most prevalent branching pattern of the LCA was bifurcation in 65.8%, while trifurcation and quadrifurcation occurred in 20.4% and 1.6%, respectively. The splitting of the RCA and absence of the LCA occurred in 4.2% and 11.8%, respectively. A significant correlation was found between the split RCA and absent LCA showing that the split RCA was more prevalent in the absence of the LCA.

The dissection of the fetal heart specimens (age range 13.13 - 26.95 weeks) found that the RCA arose from the right aortic sinus and provided arterial dominance in all the specimens. The LCA was classified into types according to their branching pattern. The bifurcation, trifurcation and quadrifurcation of the LCA occurred in 68.3%, 29.3% and 2.4% of hearts, respectively. The mean lengths of the RCA and LCA were 0.98 ± 0.54 mm and 1.83 ± 0.77 mm, respectively. The mean diameters of the RCA and LCA were 0.38 ± 0.12 mm and 0.49 ± 0.17 mm, respectively. A significant correlation was found between the RCA and LCA length and the fetal age indicating changes in the development of the coronary vasculature with fetal development.

A knowledge of the distribution of the RCA and LCA assists in providing information on the area of the myocardium supplied. With the advent of coronary angiography, a comprehensive understanding of coronary arterial anatomy and their variations is necessary.

Key Words: right coronary artery, left coronary artery, split right coronary artery, absent left coronary artery, bifurcation, trifurcation, quadrifurcation

CHAPTER 1

1.1 Introduction and Literature Review

Until the 16th century, coronary anatomical perception was predominantly influenced by the Greek and Arabic philosophical and theological principles of philosophers such as Aristotle (384-322 BC) and the physician Galen of Pergamum (129-199 AD) (Angelini *et al.*, 1999). Although, Galen initially employed the term "coronary" to the larger arteries of the heart, the first distinct account of their function occurred in 1628 when William Harvey in his *De Motu Cordis* described that the coronary arteries and veins provided the blood supply to the heart (Wearn, 1940). Leonardo da Vinci (1452-1519) briefly touched on coronary anatomy in his renowned sketches when he illustrated the aortic trifoliate valve, the right and left coronary ostia and the proximal course of the right and left coronary arteries (Figure 1) (Angelini *et al.*, 1999).

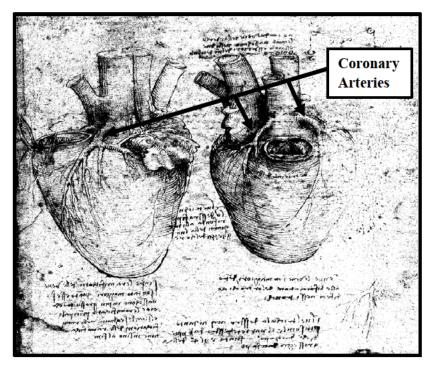


Figure 1: Leonardo da Vinci's drawings of the heart illustrating the two coronary arteries. Left: lateral view, right: frontal view (Adapted from Angelini *et al.*, 1999).

Richard Lower (1671) described the anastomoses of the branches of the coronary arteries, and Friederic Ruysch in 1704 demonstrated the distribution of their branches (Wearn, 1940). Between 1706 and 1715, R. Vieussens and A.C. Thebesius notably illustrated the connection of the chambers of the heart with the coronary vessels through the small veins and their valves (Loukas *et al.*, 2007). However, it was only in 1761 that the two main coronary vessels were precisely and definitively described by G.P. Morgagni (Angelini *et al.*, 1999).

With the dawn of the 20th century, coronary variability became the focus of anatomists and physicians prompting numerous significant publications describing the human anatomy of the coronary arteries (Angelini *et al.*, 1999). In 1962, Mason Sones introduced selective angiography whose considerable popularity encouraged awareness of coronary variability among cardiovascular specialists (Angelini *et al.*, 1999).

1.1.1 Embryological Development

1.1.1.1 Development of Blood Vessels

Blood vessels are derived from the mesodermal germ layer and are formed by either vasculogenesis or angiogenesis (Sadler, 2012). Vessels formed by vasculogenesis develop from blood islands (Figure 2) arising from induced mesodermal cells forming hemangioblasts, a common precursor for vessel formation (Sadler, 2012). However, blood vessels formed by angiogenesis involved sprouting from existing vessels (Figure 3) (Sadler, 2012).

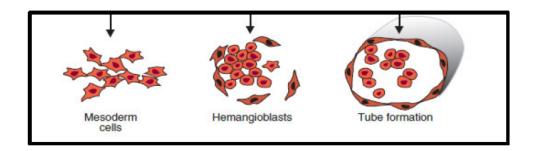


Figure 2: Illustration of Vasculogenesis (Adapted from Sadler, 2012)

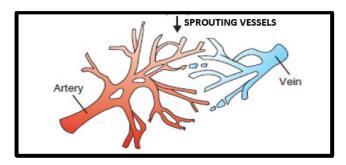


Figure 3: Illustration of Angiogenesis (Adapted from Sadler, 2012)

1.1.1.2 Development of the Coronary Circulation

During the initial stages in development of the heart, the cardiomyocytes, a fundamental cell type forming the heart are in immediate contact with the endocardium (Reese *et al.*, 2002; Ando *et al.*, 2004). At this stage, the endocardium and myocardium receives its nutrient contribution from the blood flowing through the lumen of the simple heart tube and the coronary circulation does not hitherto exist (Bernanke and Velkey, 2002; Ando *et al.*, 2004). Blood islands or vascular buds develop only after the formation of the epicardial covering of the heart (Ando *et al.*, 2004).

Coronary arteries arise from either angioblasts formed from sprouts of the sinus venosus, or the epicardium (Sadler, 2012). The transition of epicardial cells into mesenchymal cells contribute to endothelial and smooth muscle cells of the coronary arteries and these smooth muscle cells along the proximal part of the coronary arteries also receive contribution from neural crest cells (Sadler, 2012).

The origin of developing coronary arteries is a complex and debatable concept that anatomists are yet to accurately describe. Early investigations presented two prominent theories on the developing coronary arteries (Bernanke and Velkey, 2002). Initial research proposed that coronary arteries might develop as single solid cords of endothelial cells growing from the developing aortic wall at the sinus which would then form tubular channels from the aorta towards the ventricles (Bernanke and Velkey, 2002). Conversely, tubular branches at the aortic sinuses were thought to grow by angiogenesis and begin as aortic evaginations of the endothelium that become the proximal coronary arteries (Bernanke and Velkey, 2002).

The common assumption that the coronary arteries sprout from the aorta has never been demonstrated (Ando *et al.*, 2004). Anatomists have thus deduced that the proximal coronary arteries develop from the peritruncal ring of vascular tubes and grows towards the aorta (Figure 4) (Reese *et al.*, 2002; Ando *et al.*, 2004; Silva Junior *et al.*, 2009; Sadler, 2012).

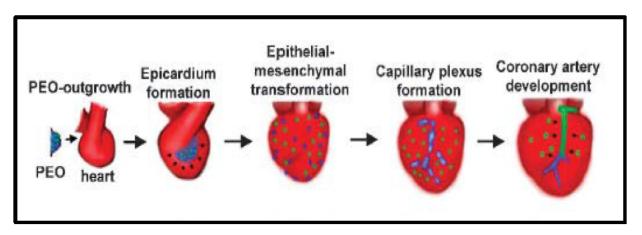


Figure 4: Illustration of the Development of the Coronary Arteries. (PEO: Proepicardial Organ) (Adapted from Reese *et al.*, 2002)

1.1.2 Coronary Artery Nomenclature

From the literature viewed, there are two categories of terminologies used in the description of the coronary arteries. Terminologia Anatomica utilizes the following terminology in describing the coronary arteries:

The RCA is used to describe the proximal trunk arising from the right aortic sinus. Its branches are the conus artery, the sinu-atrial nodal branch, the right marginal branch, the posterior interventricular branch (PIB) and the posterior left ventricular branch.

The LCA is used to describe the proximal trunk arising from the left aortic sinus. Its branches are the anterior interventricular branch (AIB), the diagonal branch, the median or intermedian branch, the circumflex artery (CX) and the left marginal branch.

Clinical and surgical literature utilize the following terminology in describing the coronary arteries (Ragosta, 2010, Moscucci, 2014):

The RCA is used to describe the proximal trunk arising from the right aortic sinus. Its branches are the conus artery, the sinus node branch, the acute marginal branch and the posterior descending artery.

The left main coronary artery is used to describe the proximal trunk arising from the left aortic sinus. Its branches are the left anterior descending artery, the left diagonal branch, the ramus intermedius or ramus medianus, the left circumflex artery and the obtuse marginal branch.

The distinction between the anatomical and clinical terminologies is presented in Table 1. This dissertation utilised anatomical terminology.

Anatomical Terminology	Clinical Terminology
(Terminologia Anatomica, 1998)	(Ragosta, 2010, Moscucci, 2014)
Right coronary artery	Right coronary artery
Conus artery	Conus artery
Sinu-atrial nodal branch	Sinus node artery
Right marginal branch	Acute marginal branch
Posterior interventricular branch	Posterior descending artery
Left coronary artery	Left main coronary artery
Anterior interventricular branch	Left anterior descending artery
Diagonal branch	Left diagonal branch
Median / Intermedian branch	Ramus intermedius /
	ramus medianus
Circumflex artery	Left circumflex artery
Left marginal branch	Obtuse marginal branch

 Table 1: Coronary artery nomenclature

1.1.3 Anatomy of the Coronary Arteries

1.1.3.1 Origin of the Coronary Arteries

Angelini *et al.* (1999) described a coronary artery as any artery or arterial branch that carries blood to the myocardium, semilunar and atrioventricular valves. In addition, it supplies the great vessels and the epicardium. Descriptive coronary anatomy has frequently overlooked the aortic root which provides the point of origin for the coronary arteries (Angelini *et al.*, 2002). The aortic root functions as the supporting structure for the aortic valve by forming the outflow tract of the left ventricle (Anderson, 2000). The aortic root comprises three semilunar leaflets, three intercuspal spaces, and three aortic root from the ascending aorta (Angelini *et al.*, 1999). At or below the level of the sinotubular junction, two of the aortic sinuses give rise to the coronary arteries (Figure 5) (Anderson, 2000). These two sinuses are defined as the right and left aortic sinuses with reference to the arrangement of the coronary arteries (Anderson, 2000).

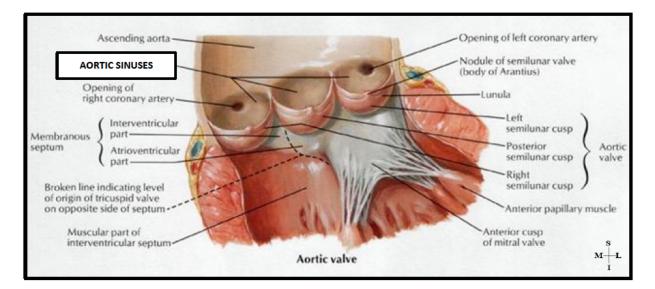


Figure 5: Illustration of the aortic valve showing the aortic sinuses (Adapted from Netter, 2006)

1.1.3.2 The Right Coronary Artery

Origin and Course

Just below the sinotubular junction, the RCA arises from an ostium in the middle of the right aortic sinus and courses into the right atrioventricular groove providing branches to the right ventricular wall (Angelini *et al.*, 1999). Between the right auricle and pulmonary trunk where the sinus bulges, the RCA passes anteriorly and marginally to the right descending in the atrioventricular groove and curving around the cardiac border into the posterior part of the groove (Standring *et al.*, 2016). The artery then reaches the interatrial and interventricular junction termed the crux of the heart, where it ends slightly to the left, frequently anastomosing with the CX artery (Standring *et al.*, 2016).

Branches and Distribution

The branches of the RCA predominantly supply the right atrium and ventricle (Figure 6) (Standring *et al.*, 2016). The first branch, the conus artery, originates from either the RCA or directly from the right aortic sinus (Pannu *et al.*, 2003). Running superiorly and posteriorly, the sinu-atrial nodal artery often arises from the proximal RCA (Pannu *et al.*, 2003). Several anterior ventricular branches then ramify toward the apex (Standring *et al.*, 2016). The right marginal artery arises at the junction of the mid and distal RCA and when very large, the remaining anterior ventricular branches may be diminished to one or may even be absent (Pannu *et al.*, 2003; Standring *et al.*, 2016). As the RCA reaches the crux, it divides into the PIB and posterior left ventricular branches (Pannu *et al.*, 2003; Standring *et al.*, 2016). In

instances where the left AIB is small, the PIB can extend around the apex to supply one third of the anterior interventricular septum (Pannu *et al.*, 2003). Arterial dominance is provided by the coronary artery which gives rise to the PIB and this is usually the RCA (Figure 7A) (Standring *et al.*, 2016). Septal branches then arise from the PIB and supply the posterior interventricular septum (Standring *et al.*, 2016). Small recurrent atrioventricular branches from the ventricular branches of the RCA supply the adjoining atrial myocardium (Figure 6) (Standring *et al.*, 2016).

1.1.3.3 The Left Coronary Artery

Origin and Course

Proximal to the sinotubular junction and above the level of the free edge of the open aortic cusp, the LCA arises from the middle portion of the left aortic sinus (Angelini *et al.*, 1999). The LCA passes between the pulmonary trunk and left atrial auricle to reach the atrioventricular groove where it divides into two or three main branches (Standring *et al.*, 2016).

Branches and Distribution

Larger in magnitude than the RCA, the LCA supplies a greater expanse of myocardium, including almost all of the left ventricle and atrium (Figure 6) (Standring *et al.*, 2016). At the atrioventricular groove, the LCA typically bifurcates into the left AIB and the left CX arteries (Pannu *et al.*, 2003). However, in some cases, a median or intermedian artery can arise from the LCA or the proximal part of the AIB or CX arteries (Chougule *et al.*, 2014; Beg *et al.*, 2015). The LCA continues as the AIB which terminates near the apex of the heart after passing through the anterior interventricular groove (Pannu *et al.*, 2003). The AIB provides diagonal and septal branches to the anterior free wall of the left ventricle and the anterior interventricular septum, respectively (Pannu *et al.*, 2003).

The CX artery runs in the left atrioventricular groove towards the crux of the heart (Angelini *et al.*, 1999; Pannu *et al.*, 2003). It provides left marginal branches to the lateral left ventricle (Pannu *et al.*, 2003). In its course, if the CX artery reaches the crux and produces the PIB, the LCA is defined as the dominant artery of the heart (Figure 7B) (Angelini *et al.*, 1999). Co-dominance occurs when both the CX and the RCA provide a PIB (Figure 8) (Parikh *et al.*, 2012; Lin *et al.*, 2015).

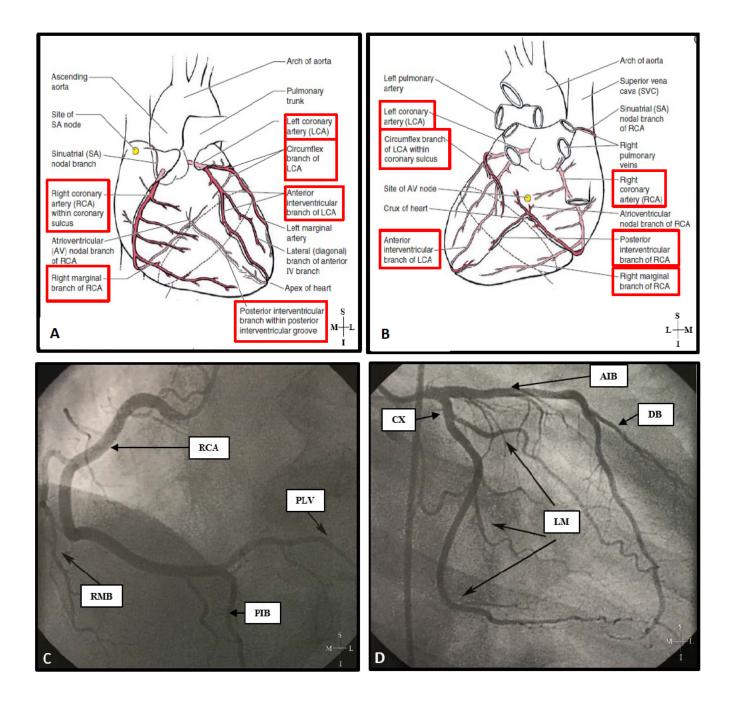


Figure 6: Illustration of the RCA, LCA and their branches in anterior view (A) and posteroinferior view (B) (Adapted from Moore *et al.*, 2010). Angiographic images showing RCA and its branches in left anterior oblique view (C) and the LCA and its branches in right anterior oblique view (D) (Adapted from Ragosta, 2010).

Common Key – RCA: right coronary artery, LCA: left coronary artery, RMB: right marginal branch, PIB: posterior interventricular branch, PLV: posterior left ventricular branch, AIB: anterior interventricular branch, CX: circumflex artery, LM: left marginal branches, DB: diagonal branch, S: superior, I: inferior, L: lateral, M: medial

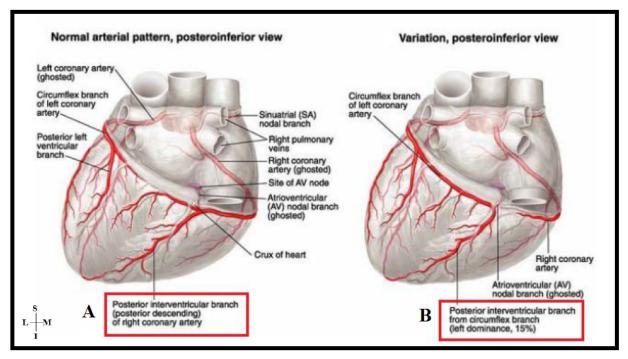
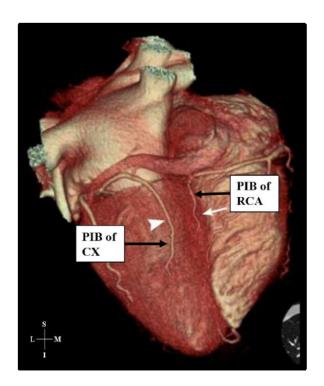
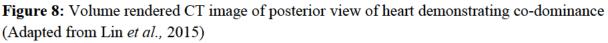


Figure 7: Illustration of a Dominant RCA (A) and Dominant LCA (B) (Adapted from Tank and Gest, 2008).





Common Key – RCA: right coronary artery, LCA: left coronary artery, CX: circumflex artery, PIB: posterior interventricular artery, S: superior, I: inferior, L: lateral, M: medial

1.1.4 Variations of the Coronary Arteries

1.1.4.1 Double or Split Right Coronary Artery

The double or split RCA is one of the rarest variations of the RCA (Karaosmanoglu *et al.*, 2008; Akcay *et al.*, 2010; Chen *et al.*, 2012). Various concepts defining a double or split RCA have been described in the literature by authors such as Gupta *et al.* (1987), Nair *et al.* (2005), Kunimasa *et al.* (2007) and Lemburg *et al.* (2007).

Gupta *et al.* (1987) reported the first incidence of a double RCA in which the two vessels arose from separate coronary ostia (Figure 9) with one vessel continuing as the right marginal branch and the other vessel continuing as the PIB. Erbagci *et al.* (2006) and Lemburg *et al.* (2007) also described a double RCA as two vessels arising from separate coronary ostia and having similar diameters. Nair *et al.* (2005) and Kunimasa *et al.* (2007) both described a double RCA arising from a single coronary ostium (Figure 10). However, Nair *et al.* (2005) found both vessels of the RCA running parallel in the right atrioventricular groove and crossing to the crux of the heart, whereas, Kunimasa *et al.* (2007) described both vessels as running in the interventricular sulcus but not reaching the crux. Misuraca and Balbarini (2010) described a double RCA as arising from a single proximal trunk (Figure 11) or separate ostia and exhibiting either a single PIB or two distinct PIB's. Conversely, Sawaya *et al.* (2008) and Andreou (2010) described split branches of the PIB forming a double or split RCA.

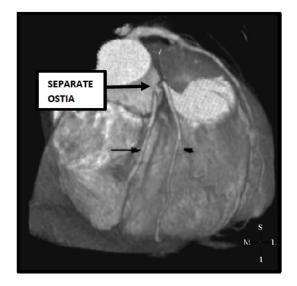


Figure 9: Volume rendered coronary CT angiographic image showing a double RCA arising from separate ostia. (Black arrows showing separate RCA branches) (right lateral view) (Adapted from Karaosmanoglu *et al.*, 2008)

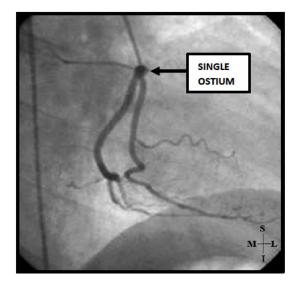


Figure 10: Angiographic image showing a double RCA arising from a single ostium (right anterior oblique view) (Adapted from Erbagci *et al.*, 2006)

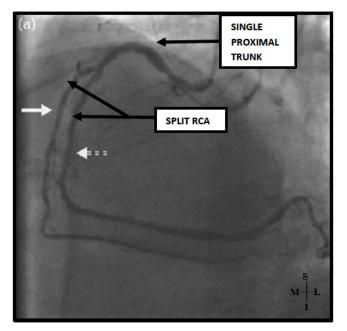


Figure 11: Angiographic image showing a RCA that splits after a proximal trunk (white arrows showing separate RCA branches) (left anterior oblique view) (Adapted from Andreou, 2010)

Common Key (Figures 9, 10, 11) – RCA: right coronary artery, black and white arrows: separate RCA branches, S: superior, I: inferior, L: lateral, M: medial

1.1.4.2 Shape of the RCA

The RCA was found to display two different geometric shapes using coronary angiography namely *C*-shaped and *Sigma* shaped (*S*-shaped) (Figure 12) (Dvir *et al.*, 2003; Gungor *et al.*, 2014). Dvir *et al.* (2003) suggested that *S*-shaped RCAs have a lower susceptibility to atherosclerosis due to the hemodynamics of blood flow in the vessels. Whereas, *C*-shaped RCA's are associated with atherosclerosis and coronary artery disease (Dvir *et al.*, 2003; Gungor *et al.*, 2003; Gungor *et al.*, 2003; Market and State at the state of blood flow in the vessels. Whereas, *C*-shaped RCA's are associated with atherosclerosis and coronary artery disease (Dvir *et al.*, 2003; Gungor *et al.*, 2014).

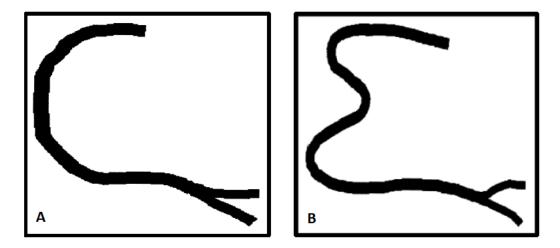


Figure 12: Illustration showing *C*-shaped (A) and *Sigma* shaped (*S*-shaped) (B) RCA (Adapted from Dvir *et al.*, 2003)

1.1.4.3 Absent Left Coronary Artery

Absence of the LCA is a variation whereby the proximal segment of the LCA, before it divides into its branches, fails to occur. This variation is characterised by the AIB and CX arteries arising directly from the left coronary ostium (Figure 13) (Kim *et al.*, 2006; Angelini *et al.*, 1999). The branching pattern of the AIB and CX arteries are otherwise typical and this variation is more prevalent in LCA dominance and aortic valvular disease (Yamanaka *et al.*, 1990; Ilia and Weinstein, 1998). Secondary absence of the LCA occurs when the AIB and CX arteries originate ectopically (Angelini *et al.*, 1999).



Figure 13: Oblique volume rendered image of the superior view of the heart showing absent LCA with separate origins of the AIB (straight arrow) and CX (curved arrow) (Adapted from Kim et al., 2006)

Key: A: aorta, PA: pulmonary artery, straight black arrow: anterior interventricular branch, curved black arrow: circumflex artery, L: lateral, M: medial

1.1.5 Clinical Relevance

Understanding the variability of their functional repercussion is one of the most significant clinical challenges presented by coronary anomalies (Angelini *et al.*, 2002). Some anomalies can be benign, whereas, other anomalies can be potentially lethal and associated with major congenital heart diseases (Angelini *et al.*, 2002; Schmitt *et al.*, 2005).

Double RCA anomalies can predispose to atherosclerotic lesion development, thereby resulting in acute coronary syndromes such as inferior myocardial infarction (Akcay *et al.*, 2010). An in depth knowledge of this anomaly may alter the management strategies in patients with coronary arterial diseases (Akcay *et al.*, 2010). Absence of the LCA can cause technical difficulties in coronary artery catheterization and may be responsible for complications or misdiagnosis (Kosar *et al.*, 2009). In contrast, patients with an absent LCA may not develop the most severe form of coronary disease such as LCA stenosis (Angelini *et al.*, 1999). With the advent of coronary arteriography and coronary artery bypass graft surgery, comprehensive understanding of coronary arteries and their anomalies has become imperative.

This study aimed to:

- Document the relationship between the morphology of the RCA and LCA.
- Examine the embryologic relationship between the proximal RCA and proximal LCA.

The objectives were to:

- Determine the relationship between the morphologic patterns of the LCA and the RCA using coronary angiograms.
- Document the branching patterns of the RCA and LCA in a Durban metropolitan region.
- Document the prevalence of split or double RCA in coronary angiograms.
- Document the prevalence of absent LCA in coronary angiograms.
- Examine the relationship of the embryology of the LCA and RCA in human fetal specimens.

1.2 Materials and Methods

The present study included analysis of human adult angiograms and an anatomical dissection of human fetal hearts.

1.2.1 Coronary Angiography

Diagnostic coronary angiography is one of the most routinely performed procedures and the principal component of cardiac catheterization (Ragosta, 2010; Moscucci, 2014). It permits the examination of the coronary tree in its entirety, whilst simultaneously documenting details such as the arterial distribution pattern, anatomic or functional pathology and the presence of collateral connections (Moscucci, 2014).

This study included a review of 500 human coronary angiograms acquired from the cardiac catheterisation laboratory of a private hospital in Kwazulu Natal, Durban, South Africa. Of these angiograms, 293 were males and 207 were females with a population group distribution of 354 Indian, 103 White and 43 Black patients. The branching patterns of the LCA and RCA were documented, including coronary arterial dominance. The RCA was divided into types using an original classification system formulated by the authors. The types were classified according to the absence or presence of a split RCA and the arterial dominance. The LCA was classified into types adapted from Tomar *et al.* (2013) and Chougule *et al.* (2014). The types were classified according to the branching pattern and the absence or presence of the LCA. The shape of the RCA was also documented and classified as either *C*-shaped or *S*-shaped, adapted from Gungor *et al.* (2014). The relationship of the anatomy of the RCA and LCA was evaluated. In addition, the presence of coronary variations such as double or split RCA and absence of the LCA was documented.

1.2.2 Anatomical Dissection

A sample of 50 fetal heart specimens were dissected at the Department of Clinical Anatomy, University of Kwazulu-Natal, Westville campus in accordance with the National Health Act no 61 of 2003. Using a Digital Vernier caliper (150mm) (Mitutoyo Digimatic Caliper Series 500, USA) the fetal foot length was measured and the age (in weeks) was then estimated using the formula y = 7.130 + 0.503x, where y = gestational age in weeks and x = foot length in mm (Pandey *et al.*, 2015). The lengths and diameters of the RCA and LCA were measured and the branching patterns and the relationship between the development of the RCA and the LCA was examined.

1.2.3 Statistical Analysis

Statistical analysis was performed using Stata 13.0 SE (StataCorp. 2013). Stata Statistical Software: Release 13. College Station, TX: StataCorp LP. Pearson's chi-squared test was implemented and a p value of less than 0.05 was deemed statistically significant. For the

angiographic results, the Pearson chi-squared test was performed to determine the association of the absence or presence of a split RCA with the absence or presence of the LCA; a split RCA with sex and population groups and; between the absence or presence of the LCA with sex and population groups. The fetal results employed the Pearson product-moment correlation test between the gestational age and the lengths and diameters of the RCA and LCA, and a p value of less than 0.05 was also deemed statistically significant. Ethical clearance was obtained from the Biomedical Research Ethics Committee of the University of Kwazulu-Natal (BE044/15).

1.3 Outline of Dissertation

Chapter 1: This chapter outlined a literature review of the coronary arteries and a brief methodology.

Chapter 2: Section 2.1 documented the morphology of the coronary arteries using coronary angiograms. In addition, variations such as split or double RCA and absence of the LCA was documented and the relationship between the right and left coronary arteries was investigated. Section 2.2 examined the embryologic relationship between the morphology of the RCA and LCA using dissected fetal heart specimens. This included branching patterns, dominance, lengths and diameters of the coronary arteries.

Chapter 3: Discussion and conclusion of the overall dissertation together with the references and appendices.

CHAPTER 2

2.1 Scientific Manuscript 1

The following manuscript was written according to the author guidelines for the journal Folia Morphologica, and has been accepted for publication (manuscript ID: 48568). This chapter investigated the relationship between the morphology of the coronary arteries using angiographic analysis. Branching patterns and arterial dominance of the RCA and LCA was documented. Furthermore, variations such as split or double RCA and absence of the LCA was also recorded. Both the RCA and LCA were classified into types according to their branching patterns and arterial dominance. The RCA was categorised into types according to the absence or presence of a split RCA and the arterial dominance. The LCA was categorised into types included bifurcation, trifurcation and quadrifurcation of the LCA. In addition, the prevalence of a split or double RCA with concomitant absence of the LCA was also documented. Cardiovascular diseases are the leading cause of death, therefore, an in-depth understanding of the morphology of the coronary arteries is beneficial.

Title: Anatomic study of the morphology of the right and left coronary arteries

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Abstract

Arising from the aorta, the right (RCA) and left (LCA) coronary arteries provide the arterial supply to both the atria and the ventricles of the heart. An extensive literature review revealed that most studies have either evaluated the morphology of the RCA or the LCA independently. This study aimed to document the relationship between the morphology of the RCA and LCA using coronary angiograms. In addition, variations such as split or double RCA and an absent LCA was documented. A review of 500 coronary angiograms was conducted and the RCA and LCA were classified according to their branching patterns and arterial dominance. The most prevalent branching pattern of the LCA was bifurcation in 65.8% ($^{329}/_{500}$), while trifurcation and quadrifurcation occurred in 20.4% ($^{102}/_{500}$) and 1.6% ($^{8}/_{500}$), respectively. The LCA was absent in 11.8% ($^{59}/_{500}$) of cases with the bifurcation and trifurcation of its branches in 10.8% $(^{54}/_{500})$ and 1.4% $(^{7}/_{500})$, respectively. The splitting of the RCA occurred in 4.2% $(^{21}/_{500})$ of the angiograms. A split RCA with concomitant absent LCA was documented in 1.2% ($^{6}/_{500}$) of the angiograms. The RCA and LCA were dominant in 77.2% ($^{386}/_{500}$) and 9.8% ($^{49}/_{500}$) of cases respectively, whereas co-dominance occurred in 13% ($^{65}/_{500}$) of the sample examined. In most cases where a split RCA was present, the RCA was found to be non-dominant. With the advent of coronary arteriography, a comprehensive understanding of coronary arterial anatomy and their anomalies has become essential.

Key Words: right coronary artery; left coronary artery; split right coronary artery; absent left coronary artery

Introduction

The heart has its own unique arterial supply provided by the coronary arteries [24]. Branching from the aorta, the RCA and LCA supply the myocardium and epicardium of the heart [24]. Arising from the right aortic sinus, the RCA descends in the coronary sulcus [24]. The RCA gives off a right marginal branch, running towards the apex of the heart, before proceeding to the posterior aspect of the heart [24]. The RCA then passes through the crux (interatrial and interventricular junction) of the heart and gives rise to the posterior interventricular branch (PIB), before terminating in the coronary sulcus [24].

Arising from the left aortic sinus, the LCA traverses the coronary sulcus for a short distance before dividing into two or three branches at the atrioventricular groove [24, 29]. The anterior interventricular branch (AIB) of the LCA runs towards the apex and gives off a diagonal branch. The circumflex branch (CX) of the LCA gives off a left marginal branch and then terminates on the posterior aspect before reaching the crux [24]. The coronary artery from which the PIB arises is referred to as the dominant artery, and it is usually the RCA (60%) [29]. Co-dominance (2.5%) occurs when both the CX and the RCA provide a PIB [6]. The posterior part of the ventricular septum and often part of the posterioal wall of the left ventricle is supplied by the PIB [29].

One of the rarest congenital anomalies of the coronary arteries is the double or split RCA [2, 11]. There is still controversy with respect to the definition and correct diagnosis of the split RCA [2]. The double or split RCA has been described by several proposed concepts [11].

Gupta *et al.* (1987) was the first to report incidence of a double RCA [23]. In their study, the two vessels arose from separate adjacent coronary ostia with the smaller vessel providing the PIB and the larger vessel continuing as the right marginal branch [23]. Nair *et al.* (2005) described a double RCA arising from a single coronary ostium where both vessels of the RCA ran parallel in the right atrioventricular groove and crossed the crux of the heart [26]. In 2007, Kunimasa *et al.* described a double RCA arising from a single ostium and supplying blood to the interventricular septum [22]. Both vessels coursed in the interventricular sulcus but did not cross the crux [22]. Lemburg *et al.* (2007) described a true double RCA, of which both vessels had similar diameters and originated from two separate adjacent coronary ostia in the right coronary sinus [23].

Double RCA were also described as two separate branches of the RCA in the atrioventricular groove running closely together for half the course of the RCA [23]. In addition, the double RCA can originate from a single proximal trunk or separate orifices from the right aortic sinus and can exhibit two distinct PIB's or a single PIB [25]. Sawaya *et al.* (2008) and Andreou (2010) described the double or split RCA as containing only split portions of the PIB, not two RCAs, with separate proximal courses [5, 27].

Certain geometric features may predispose vasculature to atherogenesis due to their effect on the local flow field [14]. Two different geometric shapes of the RCA, viz *C*-shaped and *sigma* shaped (*S*-shaped), have been described using coronary angiography [14, 17]. *C*-shaped RCA's have been found to be associated with atherosclerosis in their proximal-middle region [14]. In this proximal-middle area, the flow pattern is characterised by low shear stress along the inner wall and maximal difference of shear stress between the inner and outer walls hence making it an apt environment for the formation of atherosclerotic plaques [14]. Dvir *et al.* (2003) found *C*-shaped RCA's to be more associated with atherosclerosis than *S*-shaped RCA's due to the geometrical disposition of the *C*-shaped RCA [14].

The LCA usually divides into two branches; however, a third branch known as the median or intermedian artery is known to exist [8, 12]. The median artery can arise from the LCA or the proximal part of the AIB or CX arteries [8, 12]. It traverses the sternocostal surface of the left ventricle and is distributed around the middle area between the base and apex of the heart [8, 12].

Isolated absence of the LCA occurs when the AIB and CX arteries arise directly from the left aortic sinus as opposed to bifurcating from a common trunk [6]. The distribution patterns of the vessels are otherwise normal and this anomaly is more prevalent in the presence of aortic valvular disease and LCA dominance [20, 31]. Instances where the AIB and CX arteries originate outside the left coronary sinus or ectopically is known as secondary absence of the LCA [6].

This study aimed to document the relationship between the morphology of the RCA and LCA, including their branching patterns and the shape of the RCA. In addition, the prevalence of split or double RCA and absence of the LCA was documented using coronary angiograms.

Materials and Methods

This retrospective study included a review of 500 human coronary angiograms acquired from the cardiac catheterisation laboratory of a private hospital in KwaZulu Natal, Durban, South Africa. Of these angiograms, 293 were males and 207 were females with a population group distribution of 354 Indian, 103 White and 43 Black patients. The branching patterns of the LCA and RCA were documented, including coronary arterial dominance. The RCA was divided into types using an original classification system formulated by the authors. The types were classified according to the absence or presence of a split RCA and the arterial dominance. RCA Type A occurred when a single RCA was present, Type B was a split RCA with left dominance, Type C was a split RCA with co-dominance and Type D was a split RCA with right dominance. The LCA was classified into types adapted from Tomar et al., (2013) and Chougule et al., (2014) [12, 30]. The types were classified according to the branching pattern and the absence or presence of the LCA. The LCA Type A occurred when the LCA bifurcated into AIB and CX arteries, Type B occurred when the LCA trifurcated into AIB, median and CX arteries, Type C was categorised as quadrifurcating into AIB, two median arteries and a CX artery, Type D occurred when the LCA was absent and the AIB and CX arteries originated separately from the aortic sinus and Type E occurred when the LCA was absent and the AIB, median and CX arteries arose from the left aortic sinus.

The shape of the RCA was also documented and classified as either *C*-shaped or *S*-shaped adapted from Gungor *et al.*, 2014 [17]. The relationship of the anatomy of the RCA and LCA was evaluated. In addition, the presence of coronary variations such as double or split RCA and absence of the LCA was documented. The RCA was classified as double or split when two separate branches of the RCA were found running together for at least half the course of the RCA [23]. A split RCA could originate from either a single proximal trunk or separate orifices [25].

Statistical analysis was performed using Stata 13.0 SE (StataCorp. 2013). Stata Statistical Software: Release 13. College Station, TX: StataCorp LP. Pearson's chi-squared test was implemented and a p value of less than 0.05 was deemed statistically significant. Ethical clearance was obtained from the Biomedical Research Ethics Committee of the University of Kwazulu-Natal (BE044/15).

Results

The RCA and LCA were each classified into types according to their branching patterns, arterial dominance and the absence or presence of the LCA and split RCA (Table 1).

Right Coronary Artery (RCA)

A single RCA (Type A) was present in 95.8% ($^{479}/_{500}$) and a split RCA was found in 4.2% ($^{21}/_{500}$) of cases. Type B (split RCA with left dominance) occurred in 3.6% ($^{18}/_{500}$) of cases. Type C (split RCA with co-dominance) was present in 0.4% ($^{2}/_{500}$) of cases, while Type D (split RCA with right dominance) occurred in 0.2% ($^{1}/_{500}$) of cases (Table 1).

Left Coronary Artery (LCA)

The LCA was present in 88.2% (⁴⁴¹/₅₀₀) and absent in 11.8% (⁵⁹/₅₀₀) of the sample examined. The LCA was divided into types according to its branching patterns, arterial dominance and absence or presence of the LCA. When the LCA was present; LCA Type A (bifurcation of the LCA) occurred in 65.8% (³²⁹/₅₀₀) of cases. Type B (trifurcation of the LCA) occurred in 20.4% (¹⁰²/₅₀₀) of cases and Type C (quadrifurcation of the LCA) had a prevalence of 1.6% (⁸/₅₀₀). When the LCA was absent; Type D (bifurcation) occurred in 10.8% (⁵⁴/₅₀₀) of cases and Type E (trifurcation) was recorded in 1.4% (⁷/₅₀₀) (Table 1). When the LCA was present, split RCA occurred in 3.4% (¹⁵/₄₄₁) and when the LCA was absent, split RCA occurred in 10.2% (⁶/₅₉).

In 85.2% ($^{426}/_{500}$) angiograms, a single RCA occurred with an LCA presenting normal coronary anatomy. This occurred in 87% ($^{255}/_{293}$) males and 84% ($^{174}/_{207}$) females. A single RCA with an absent LCA occurred in 10.6% ($^{53}/_{500}$) of the angiograms and this occurred in 10.2% ($^{30}/_{293}$) males and 11% ($^{23}/_{207}$) females. The splitting of the RCA with the LCA present occurred in 3% ($^{15}/_{500}$) of angiograms (Figure 1). This occurred in 3.4% ($^{10}/_{293}$) males and 3.4% ($^{5}/_{207}$) females. The concomitant splitting of the RCA with an absent LCA occurred in 1.2% ($^{6}/_{500}$) of the angiograms (Figure 2). This occurred in 0.3% ($^{1}/_{293}$) male and 3.4% ($^{5}/_{207}$) females. With respect to the shape of the RCA, 68% ($^{340}/_{500}$) was found to be *C*-shaped and 32% ($^{160}/_{500}$) *S*shaped. *C*-shaped occurred in 66.6% ($^{195}/_{293}$) males and 70% ($^{145}/_{207}$) females and *S*-shaped occurred in 33.4% ($^{98}/_{293}$) males and 29.9% ($^{62}/_{207}$) females.

The Pearson chi-squared test between the absence or presence of a split RCA and the absence or presence of the LCA presented a p value of 0.015. The chi-squared test between a split RCA and sex and population groups revealed p values of 0.554 and 0.063, respectively. The chi-

squared test between the absence or presence of the LCA and sex and population groups revealed p values of 0.314 and 0.772, respectively (Table 2).

Discussion

An extensive literature review revealed that most studies have either evaluated the anatomic variations of the RCA or LCA independently. This study found an incidence of 4.2% for double or split RCA and when compared to the literature corresponded more closely to Angelini *et al.* (1999) who documented 1.23%, and was much higher than that of Erbagci *et al.* (2006) and Kunimasa *et al.* (2007) who found 0.01% and 0.07%, respectively [6, 15, 22]. However, due to its rarity, the split RCA is more frequently described in case reports (Table 3).

The incidence of absent LCA in the present study was 11.8%. This was similar to the study by Ajayi *et al.* (2015) who reported an incidence of 9.6% of an absent LCA [1]. However, this incidence is considerably higher than Yamanaka *et al.* (1990) (0.41%), Angelini *et al.* (1999) (0.47%) and Altin *et al.* (2015) (0.9%) (Table 4) [3, 6, 31].

This study, however, aimed to investigate the RCA in conjunction with the LCA, with a focus on a split RCA and absent LCA. The Pearson Chi Squared test showed that there is a significant correlation between the split RCA and absent LCA (p < 0.05). A split RCA occurred more often in the absence (10.2%) than the presence (3.4%) of the LCA. Bogers *et al.* (1989), showed that coronary vessels develop by ingrowth towards their orifices on the ascending aorta which differs from the previous assumption that coronary arteries are formed by outgrowths from the aorta and the systemic venous sinus, respectively [9]. Ajayi *et al.* (2015) suggested that the high prevalence of split RCA in hearts with absent LCA may be due to the occurrence of the fast ingrowth of the primitive coronary vascular network in both the left and right coronary vascular tree [1]. The branches of the RCA may have joined to form a single trunk while approaching the right coronary ostium due to fast ingrowth in such hearts. The present study corroborated their finding with the significant correlation between the absent LCA and split RCA.

The normal anatomy of the coronary arteries was present in 85.2% of hearts and the right coronary system provided the most prevalent arterial dominance which was 70.4%. Single RCA with an absent LCA was found in 10.6% of the angiograms and the RCA was dominant in 6.6%. The presence of the LCA with the splitting of the RCA occurred in 3% of the

angiograms and the LCA was dominant in 1.8% of these angiograms. The concomitant absence of the LCA with splitting of the RCA was present in 10.2% of the angiograms with absent LCA. In these cases, left dominance was observed in all hearts and this variation was observed in more females (83.3%) than males (16.6%). This was lower than Ajayi *et al.* (2015) who found 20.5% of hearts presenting a split RCA with absence of the LCA [1]. This study found left dominance to be more prevalent in the presence of a double or split RCA (85.7%).

With regard to the shape of the RCA, 68% was found to be *C*-shaped and 32% *S*-shaped. This was similar to the result of Demirbag and Yilmaz (2005) who found 65.7% *C*-shaped and 34.3% *S*-shaped [13]. It differed with the report of Dvir *et al.* (2003) who recorded *S*-shaped to be more prevalent than *C*-shaped (30% C-shaped and 70% S-shaped) as well as Gungor *et al.* (2014) who found a higher incidence of *C*-shaped (84.9% *C*-shaped and 15.1% *S*-shaped) [14, 17]. *C*-shaped RCA's have been found to be associated with atherosclerosis and coronary artery disease [14, 17]. Dvir *et al.* in 2003 postulated that the bend in the middle region of an *S*-shaped RCA accounts for a different hemodynamic pattern, and consequently a lower susceptibility to atherosclerotic disease [14].

Conclusion

This study found a significant correlation between split RCA and absent LCA with the splitting of the RCA more prevalent in the absence than presence of the LCA. With the advent of coronary angiography and cardiopulmonary bypass surgery, an in-depth knowledge of coronary arterial anatomy and associated anomalies is of great importance.

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Legends

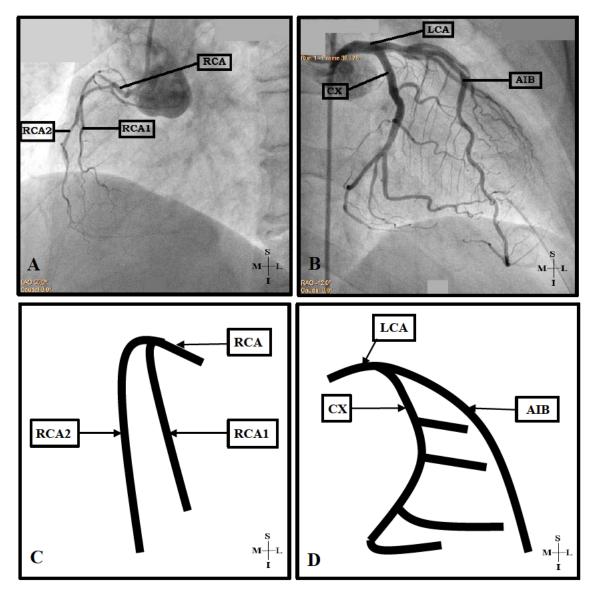


Figure 1: Angiographic images from the same patient showing a split RCA (A) and present LCA (B). Corresponding schematic diagram representing a split RCA (C) and present LCA (D). (A: left anterior oblique view, B: right anterior oblique view).

Key – RCA: right coronary artery, RCA1: right coronary artery 1, RCA2: right coronary artery 2, LCA: left coronary artery, CX: circumflex artery, AIB: anterior interventricular branch, S: superior, I: inferior, L: lateral, M: medial

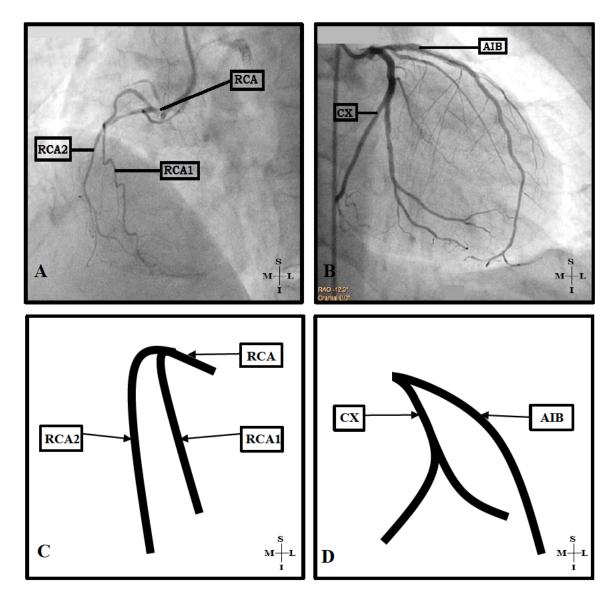


Figure 2: Angiographic images from the same patient showing a split RCA (A) and absent LCA (B). Corresponding schematic diagram representing a split RCA (C) and absent LCA (D). (A: left anterior oblique view, B: right anterior oblique view).

Key – RCA: right coronary artery, RCA1: right coronary artery 1, RCA2: right coronary artery 2, LCA: left coronary artery, CX: circumflex artery, AIB: anterior interventricular branch, S: superior, I: inferior, L: lateral, M: medial

Tables

Table 1: Classification Types of RCA and LCA

RCA Types	Description	Schematic Diagram	Incidence (%)	LCA Types	Description	Schematic Diagram	Incidence (%)
Type A	Single RCA	RCA	96	Туре А	Present Bifurcation		65.8
Type B	Split Left Dominance	RCA AIB PIB	3.4	Туре В	Present Trifurcation		20.4
Type C	Split Co- dominance	RCA LCA AIB PIB	0.4	Type C	Present Quadrifurca- tion	LCA AIB MA	1.6
Type D	Split Right Dominance	RCA LCA CX AIB	0.2	Type D	Absent Bifurcation		10.8
				Type E	Absent Trifurcation		1.4

Table 2: Data analysis showing results of Pearson chi squared tests	Table 2: Data ana	lysis showing re	esults of Pearson	chi squared tests
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Variables	Pearson Chi Squared
	Test (p value)
Absence or presence of split RCA and absence or presence of LCA	0.015
Split RCA and sex	0.554
Split RCA and population groups	0.063
Absence or presence of LCA and sex	0.314
Absence or presence of LCA and population groups	0.772

 Table 3: Incidence of double or split RCA

Author (year)	Sample Size (n)	Incidence of Double/Split RCA (%)
Angelini et al. (1999) [6]	1950	1.23
Harikrishnan et al. (2001) [18]	1 case report	-
Altun et al. (2002) [3]	2 case reports	-
Harikrishnan et al. (2002) [19]	7400	0.01
Erbagci et al. (2006) [15]	1 case report	-
Kunimasa et al. (2007) [22]	2957	0.07
Gulel et al. (2007) [16]	1 case report	-
Sawaya et al. (2008) [27]	1 case report	-
Akcay et al. (2010) [2]	1 case report	-
Selcoki et al. (2010) [28]	2 case reports	-
Present study	500	4.2

Table 4: Incidence of absent LCA

Author (year)	Sample Size (n)	Incidence of Absent LCA
Ilia et al. (1998) [20]	126 595	0.41
Angelini et al. (1999) [6]	1950	0.67
Cankaya et al. (2009) [10]	1 case report	-
Kosar et al. (2009) [21]	700	0.4
Ajayi et al. (2015) [1]	407	9.6
Present study	500	11.8

2.2 Scientific Manuscript 2

The following paper has been written according to the author guidelines for the International Journal of Morphology, and is currently under review. The relationship between the morphology of the RCA and LCA was investigated using coronary angiograms in Chapter 2. This chapter examined the embryologic relationship between the morphology of the coronary arteries using dissected fetal heart specimens. The lengths and external diameters of the RCA and LCA was also documented. The branching patterns and arterial dominance of the RCA and LCA was also documented. The LCA was classified into types according to the absence or presence of a median artery. These types included bifurcation, trifurcation and quadrifurcation of the LCA. Knowledge of the morphological characteristics including the distribution of the coronary arteries assists in providing information on the development of the coronary arteries and the area of the myocardium supplied.

 Title:
 Morphologic relationship between the coronary arteries during fetal development

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Abstract

A detailed understanding of the coronary arteries is of paramount importance in the management of coronary arterial diseases. The arterial supply to the heart originates from right (RCA) and left (LCA) coronary arteries which form an oblique inverted crown within the atrioventricular groove. This study aimed to document the embryologic relationship between the RCA and the LCA including their lengths, diameters, branching patterns and arterial dominance in fetuses. Forty-one human fetal heart specimens with an age range of 13.13 to 26.95 weeks were dissected at the Department of Clinical Anatomy, University of Kwazulu-Natal, Durban, South Africa. The RCA arose from the right aortic sinus and was dominant in all the specimens. The LCA was classified into types according to their branching pattern. The bifurcation, trifurcation and quadrifurcation of the LCA occurred in 68.3%, 29.3% and 2.4% of hearts, respectively. The mean lengths of the RCA and LCA were 0.98 \pm 0.54mm and 1.83 \pm 0.77mm, respectively. The mean external diameters of the RCA and LCA were 0.38 \pm 0.12mm and 0.49 \pm 0.17mm, respectively. There was a significant correlation between the RCA and LCA length and the fetal age which is indicative of significant changes in the coronary vasculature with fetal growth.

Key Words: right coronary artery, left coronary artery, branching patterns, bifurcation, trifurcation, quadrifurcation

Introduction

Early embryonic circulation is symmetrical and is modified throughout development [28]. The formation of the coronary arteries begins in the third week and involves a series of carefully regulated events including vasculogenesis, angiogenesis, arteriogenesis and remodelling [25, 29]. The embryonic coronary arteries have been described by two definitions of physiological development [25]. It was initially assumed that the coronary arteries were formed by outgrowths from the aorta, however, this has never been documented [4]. Bogers *et al.* (1989) reported that coronary arteries develop through ingrowth of the vessels by demonstrating that the coronary arteries could be identified in the walls of the aortic sinuses before the formation of the coronary orifices [7]. It is now largely accepted that the proximal coronary arteries develop from a complex capillary network derived from epicardial mesenchyme and not as sprouting and branching outgrowths of the aorta [24].

The RCA and LCA provide the arterial supply to the heart by forming an oblique inverted crown within the atrioventricular groove [17, 28]. The major branches of the coronary arteries are typically subepicardial, however, those in the coronary sulcus are deeply sited and frequently embedded in the myocardium [27, 28]. Anastomoses of the right and left coronary arteries occur frequently in the fetus but decreases by the end of the first year [28]. A dominant artery refers to the coronary artery providing the posterior interventricular branch (PIB) which supplies the posterior ventricular septum and frequently part of the posterolateral wall of the left ventricle [22]. The RCA is usually dominant with varying incidence ranging from 55% to 89.6% [3, 5, 13, 15, 28].

Right Coronary Artery

Arising from the right aortic sinus, the RCA runs in the coronary sulcus between the right atrium and right ventricle [10]. The first branch of the RCA is usually the right conal artery, however, this artery arises independently in one third of hearts [28]. Descending in the coronary sulcus, the RCA gives off anterior atrial and ventricular branches that diverge widely [26]. A branch running toward the apex of the heart, termed the right marginal artery is greater in calibre than other anterior ventricular arteries [27]. At the posterior aspect of the heart, the RCA passes through the junction of the interatrial and interventricular septa between the four heart chambers (the crux) and gives rise to up to three small interventricular branches including the PIB [28]. The PIB descends toward the apex in the posterior interventricular groove and supplies the posterior interventricular septum [17, 28]. The terminal branch of the RCA, termed

the posterior left ventricular branch, then continues briefly in the coronary sulcus [17]. The RCA supplies the right chambers, some parts of the left chambers and the atrioventricular septum [10].

Left Coronary Artery

The LCA is larger in calibre and supplies a greater volume of the myocardium including the left chambers and most of the interventricular septum [27]. Originating from the left aortic sinus, the LCA passes between the left auricle and pulmonary trunk to traverse the coronary sulcus [10]. The LCA divides into two or three branches at the atrioventricular groove viz. the anterior interventricular branch (AIB) and the circumflex artery (CX) [17, 28]. The AIB continues to the apex of the heart and commonly anastomoses with the PIB of the RCA on the posterior aspect of the heart [26]. The AIB gives off right and left anterior ventricular, anterior septal and corresponding posterior branches [28]. The largest anterior ventricular branch is referred to as the diagonal artery and may be doubled [10]. The CX artery follows the coronary sulcus and terminates on the posterior aspect of the heart before reaching the crux, however, it sometimes continues as the PIB in cases of left dominance [17, 28]. The CX supplies the left ventricle by its left marginal branch [17].

In addition to the AIB and CX arteries, the LCA can give rise to one or two additional terminal branches referred to as median or intermedian arteries [8, 9]. The median artery can originate from the vertex of the angle between the AIB and CX arteries including the proximal part of the AIB and CX arteries [1, 8]. From the literature reviewed, there is paucity of reports on the anatomic relationship of the development of the RCA and the LCA in fetuses. Therefore, this study aimed to document the embryologic relationship between the proximal RCA and LCA in fetal hearts including the arterial dominance and branching patterns.

Materials and Methods

A sample of 50 human fetal heart specimens were dissected at the Department of Clinical Anatomy, University of Kwazulu-Natal, Westville campus, Durban, South Africa in accordance with the National Health Act no 61 of 2003. In 9 fetuses, the hearts presented with congenital malformations and were therefore excluded resulting in a sample size of 41 dissected hearts with an age range of 13.13 to 26.95 weeks.

Gestational age was estimated using the formula y = 7.130 + 0.503x, where y = gestational age in weeks and x = fetal foot length in mm [21]. The length and external diameter of the proximal RCA and LCA was measured with the length of the RCA measured from its origin to its first branch. The branching patterns of the RCA and LCA were documented. The relationship between the development of the RCA and the LCA was examined. The LCA was classified into types according to the branching pattern [8, 30]. The LCA Type A occurred when the artery bifurcated into AIB and CX arteries, Type B occurred when the LCA trifurcated into AIB, median and CX arteries and Type C was categorised as quadrifurcating into AIB, two median arteries and a CX artery.

Statistical analysis was performed using Stata 13.0 SE (StataCorp. 2013). Stata Statistical Software: Release 13. College Station, TX: StataCorp LP. The Pearson product-moment correlation test was implemented and a p value of less than 0.05 was deemed statistically significant. Ethical clearance was obtained from the Biomedical Research Ethics Committee of the University of Kwazulu-Natal (BE044/15).

Results

In all the specimens, the RCA arose from the right aortic sinus and traversed the coronary sulcus before giving rise to the PIB on the posterior surface of the heart. The RCA gave rise to the PIB in all cases, and therefore right dominance occurred in 100% $(^{41}/_{41})$ of cases. The LCA was divided into types according to the branching pattern. LCA Type A (bifurcation) (Figure 1) occurred in 68.3% $(^{28}/_{41})$ of specimens, Type B (trifurcation) (Figure 2) occurred in 29.3% $(^{12}/_{41})$ of cases and Type C (quadrifurcation) (Figure 3) occurred in 2.4% $(^{1}/_{41})$ of cases.

The mean length of the proximal RCA was found to be 0.98 ± 0.54 mm (range 0.3 - 2.2mm) and the mean external diameter of the RCA was found to be 0.38 ± 0.12 mm (range 0.1 - 0.6mm). The mean lengths of the LCA and its external diameter were 1.83 ± 0.77 mm (range 0.3 - 3.5mm) and 0.49 ± 0.17 mm (range 0.2 - 1.0mm), respectively (Table I). The Pearson product-moment correlation test found a significant positive association between the gestational age (in weeks) of the fetuses and the length of the LCA producing a *r* value of 0.57 and a *p* value of 0.0001. A significant positive correlation was also found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127. A positive correlation was found between the age (in weeks) and the length of the RCA with a *r* value of 0.39 and a *p* value of 0.0127.

of 0.39 and a p value of 0.0109. There was also a significant relationship between the gestational age and the diameter of the RCA resulting in a r value of 0.64 and a p value of < 0.001. In addition, there was a positive association between the lengths of the RCA and LCA with a r value of 0.42 and a p value of 0.0056. However, there was no correlation between the length and branching patterns of the LCA producing a r value of 0.17 and a p value of 0.2958 (Table II).

Discussion

Various studies regarding coronary vasculature use predominantly adult subjects, hence, little consideration has been given to fetal coronary anatomy [18]. By investigating fetal vessel dimensions, the influence of secondary factors such as atherosclerosis and arterial hypertension can be excluded [19].

In this study, the proximal RCA and LCA were present in all specimens and the absence of the LCA and split RCA was not documented. The RCA arose from the right aortic sinus and gave rise to the PIB in all the hearts. Nowak *et al.* (2008) reported on coronary vascular anatomy in fetuses and recorded right, left and co-dominant circulation as 32.5%, 38% and 29.5%, respectively [18]. This differed from the current study in which all the fetal heart specimens had right dominance. As noted earlier, from the literature reviewed, there is paucity of reports on the anatomic relationship of the development of RCA and LCA in human fetal specimens. Therefore, the results of the present study were compared to adult studies. Type A (bifurcation) occurred in 68.3% of hearts and was similar to Dattatray *et al.* (2012) (54.7%), Tomar *et al.* (2013) (76%), Ogeng'o *et al.* (2014) (54.8%) and Santhoshkumar *et al.* (2014) (70%) [9,20, 24, 30]. However, it disagreed with Kalpana (2003) who found 47% and Beg *et al.* (2015) who found 45% (Table III) [6, 12].

LCA Type B (trifurcation), occurred in 29.3% and was similar to Dattatray *et al.* (2012) (35.9%), Ajayi *et al.* (2013) (18.5%), Tomar *et al.* (2013) (24%), Ogeng'o *et al.* (2014) (32.2%) and Santhoshkumar *et al.* (2014) (26%) [1, 9, 20, 24, 30]. This differed from the results of Kulkarni *et al.* (2012) and Jaishree *et al.* (2015) who found 11.54% and 14.5%, respectively (Table III) [11, 14].

Quadrifurcation of the LCA (Type C) was recorded in 2.4% of the specimens and was similar to the reports of Ajayi *et al.* (2013) (0.7%), Santhoshkumar *et al.* (2014) (2%) and Jaishree *et*

al. (2015) (4%) [1, 11, 24]. The incidence of Type C was however lower than that of Kalpana (2003), Ogeng'o *et al.* (2014) and Beg *et al.* (2015), and who recorded 11%, 9.6% and 10%, respectively (Table III) [6, 12, 20]. Study of the distribution of the LCA aids in providing information on the area of the myocardium supplied [11]. In the case of occlusion of the CX or AIB, the additional median arteries constitute a significant source of collateral circulation to the heart [20]. This is due to the potential of these additional arteries to supply a significant area of the myocardium [20].

Since the LCA supplies a greater expanse of the heart, trifurcation of the LCA decreases left main impedance by providing a hydrodynamic advantage [16]. A large median artery can also provide electrical stability by protecting against ventricular fibrillation during acute occlusion of the AIB [16]. Conversely, a large median artery may result in the presence of diminutive diagonal or left marginal arteries [16]. A small median branch is also predisposed to atherosclerosis since it can restrict blood flow of the left main trunk [16].

The significant positive correlation between the lengths of the LCA and RCA with the fetal age indicated that there are significant changes in the development of the coronary vasculature with fetal heart development. There was also a significant association between the lengths of the RCA and LCA. However, the length of the LCA showed a higher significant correlation (r=0.57, p=0.0001) with age than the length of the proximal RCA (r=0.39, p=0.0127). This may suggest that the LCA grows faster than the RCA during fetal development. Ajayi *et al.* (2015) reported that 20.5% of the patients with absent LCA had splitting of the RCA and suggested that in such patients during development of the coronary arteries there is fast ingrowth of the primitive coronary vascular network in both the left and right coronary vascular tree [2].

The size of the coronary arteries typically determines the treatment options in the management of coronary artery disease as small arteries may cause anastomotic difficulties during bypass grafting and can influence the outcome in procedures such as stenting and balloon angioplasty [1].

Conclusion

A significant correlation between the gestational age and the lengths of the proximal RCA and LCA was recorded. This is indicative of the significant changes in the coronary vasculature with fetal growth as there is an increase in nutritional and oxygen demand.

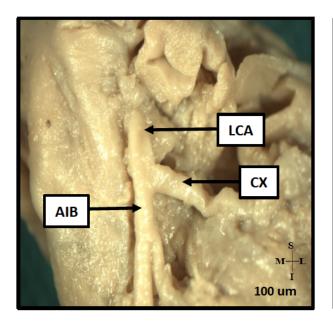
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Figures and Legends



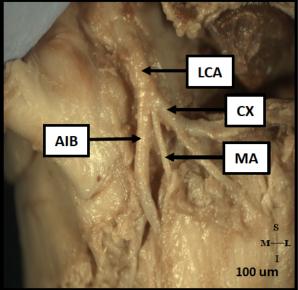


Figure 1: Bifurcation of the LCA (Type A)

Figure 2: Trifurcation of the LCA (Type B)

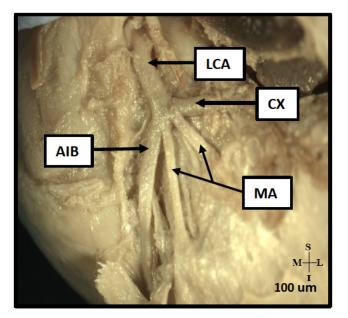


Figure 3: Quadrifurcation of the LCA (Type C)

Common Key – LCA: left coronary artery, AIB: anterior interventricular branch, CX: circumflex branch, MA: median artery, S: superior, I: inferior, L: lateral, M: medial

Tables

	Mean (mm)	Std Dev (mm)	Range (mm)
RCA Length	0.98	0.54	0.3 – 2.2
RCA Diameter	0.38	0.12	0.1 – 0.6
LCA Length	1.83	0.77	0.3 – 3.5
LCA Diameter	0.49	0.17	0.2 - 1.0

Table I: Means lengths and diameters of the RCA and LCA

Table II: Statistical analysis showing results of Pearson product-moment correlations

Variables	<i>r</i> value	<i>p</i> value
Gestational age and length of LCA	0.57	0.0001
Gestational age and length of RCA	0.39	0.0127
Gestational age and diameter of LCA	0.39	0.0109
Gestational age and diameter of RCA	0.64	< 0.001
Length of LCA and length of RCA	0.42	0.0056
Length and branching patterns of LCA	0.17	0.2958

Table III: Incidence of LCA types

Authors	Sample Size	Type A (bifurcation) (%)	Type B (trifurcation) (%)	Type C (quadrifurcation) (%)
Kalpana (2003) [12]	100	47	40	11
Dattatray et al. (2012) [9]	64	54.7	35.9	7.8
Kulkarni et al. (2012) [14]	107	-	11.54	-
Ajayi et al. (2013) [1]	151	80.8	18.5	0.7
Tomar et al. (2013) [29]	50	76	24	-
Chougule <i>et al.</i> (2014) [8]	50	35	15	-
Ogeng'o et al. (2014) [20]	208	54.8	32.2	9.6
Santhoshkumar et al. (2014) [23]	50	70	26	2
Beg et al. (2015) [6]	40	45	42.5	10
Jaishree et al. (2015) [11]	76	81.5	14.5	4
Present Study	41	68.3	29.3	2.4

CHAPTER 3

3.1 Synthesis and Conclusion

Coronary artery disease is one of the major causes of mortality. Therefore, a knowledge of the morphological characteristics and variations of the coronary arteries is imperative during diagnostic and therapeutic interventional procedures (Kalpana, 2003).

Various studies have investigated the anatomy of the coronary arteries separately; however, there is a scarcity in literature exploring a correlation between the RCA and LCA. This study therefore investigated the morphology of the RCA with its counterpart, the LCA, with emphasis on the prevalence of a split RCA and absent LCA.

3.1.1 Angiography

The RCA was found to be single in 95.8% and double or split in 4.2% of hearts. The incidence of split RCA reported in this study compared favourably with the literature reviewed (Angelini *et al.*, 1999; Erbagci *et al.*, 2006; Kunimasa *et al.*, 2007); however, double or split RCA is predominantly described in case reports due to its rarity. The split RCA is regarded as a benign congenital anomaly, although it can possibly be harmful in atherosclerosis (Sato *et al.*, 2008). Atherosclerosis of either of the split arteries may be clinically significant and misinterpretation can occur during angiography if only one artery is catheterized (Karaosmanoglu *et al.*, 2008).

The LCA was found to be present in 88.2% and absent in 11.8% of hearts. The incidence of absent LCA is higher than that reported in the literature reviewed (Yamanaka *et al.*, 1990; Angelini *et al.*, 1999; Altin *et al.*, 2015). However, it was similar to the report of Ajayi *et al.* (2015) (9.6%), who suggested that the higher incidence of the absence of the LCA can be due to it not being frequently reported or as a result of inter-population differences. The absence of the LCA could be a source of complication during diagnostic, interventional and surgical procedures (Kosar *et al.*, 2009). Although, it has no adverse hemodynamic consequences, it can cause technical difficulties in coronary artery catheterization and result in misdiagnosis (Ajayi *et al.*, 2015). Failure to interpret the absence of the LCA during catheterization may also result in misinterpretation of the LCA as being possibly totally obstructed or attetic (Ajayi *et al.*, 2015). Conversely, left main coronary artery stenosis may not develop in patients with an absent LCA (Angelini *et al.*, 1999).

When the RCA was compared with its concomitant LCA, the Pearson Chi Squared test resulted in a significant correlation between the split RCA and absent LCA (p < 0.05). A split RCA was found to occur more often in the absence (10.2%) than the presence (3.4%) of the LCA. Bogers *et al.* (1989) demonstrated that coronary vessels develop by ingrowth towards their orifices The result of the present study corroborated the findings of Ajayi *et al.* (2015) who proposed that the fast ingrowth of the primitive coronary vascular network in both the left and right coronary vascular tree may result in a higher prevalence of split RCA with an absent LCA. Therefore, the branches of the RCA may have joined to form a single trunk while approaching the right coronary ostium due to its fast ingrowth in such hearts.

With respect to the shape of the RCA, this study found a higher prevalence of *C*-shaped RCA (68%) than *S*-shaped RCA (32%) in the angiograms reviewed. The *S*-shaped RCA's have a lower susceptibility to atherosclerotic disease. Therefore, *C*-shaped RCA's have been found to be more susceptible to atherosclerosis and coronary artery disease (Dvir *et al.*, 2003; Gungor *et al.*, 2014).

3.1.2 Fetal Anatomy

The fetal specimens dissected presented a single RCA with presence of the LCA in all hearts and a split RCA or absent LCA was not observed. In all hearts, the RCA provided the main arterial dominance and coursed through the coronary sulcus exhibiting no significant variability. However, the LCA presented a variation in its branching pattern with the occurrence of one or more median arteries resulting in bifurcation, trifurcation and quadrifurcation of the LCA. From the literature reviewed, there is paucity of reports on the anatomic relationship of the development of the RCA and the LCA in fetuses. Therefore, the results of this fetal study were compared to that of adult studies.

Bifurcation of the LCA occurred in 68.3% of hearts and corroborated the results of authors such as Dattatray *et al.* (2012), Tomar *et al.* (2013), Ogeng'o *et al.* (2014) and Santhoshkumar *et al.* (2014) who found 54.7%, 76%, 54.8% and 70%, respectively. Trifucation of the LCA occurred in 29.3% of hearts which agreed favourably with Dattatray *et al.* (2012) (35.9%), Ajayi *et al.* (2013b) (18.5%), Tomar *et al.* (2013) (24%), Ogeng'o *et al.* (2014) (32.2%) and Santhoshkumar *et al.* (2014) (26%). Quadrifurcation of the LCA occurred in 2.4% of hearts and was similar to studies by Ajayi *et al.* (2013b) (0.7%), Santhoshkumar *et al.* (2014) (2%) and Jaishree *et al.* (2015) (4%).

Statistical analysis indicated a significant relationship between the development of the LCA and RCA when the lengths of the RCA and LCA were correlated with gestational age. This corroborates Ajayi *et al.*'s (2015) suggestion that there is fast ingrowth of the primitive

coronary vascular network in both the left and right coronary vascular tree during fetal development.

Understanding the anatomy and variations of the LCA provides a better knowledge of the area of the myocardium supplied (Jaishree *et al.*, 2015). The presence of a median artery has the potential to supply a substantial area of the myocardium and is therefore a considerable source of collateral circulation if the AIB or CX arteries are obstructed (Ogeng'o *et al.*, 2014). The occurrence of a median artery can also decrease left main coronary impedance by providing a hydrodynamic advantage (Mamatha *et al.*, 2014). Conversely, the size of the median artery can also have an adverse effect on the integrity of the LCA. By restricting blood flow, a smaller median artery is predisposed to atherosclerosis and a larger median artery may result in diminutive left marginal and diagonal branches (Mamatha *et al.*, 2014).

The size of the coronary arteries is also important for determining the treatment options in the management of coronary artery disease (Ajayi *et al.*, 2013b). The length of the LCA can alter hemodynamic flow and may therefore affect the distribution of atherosclerotic lesions in its branches (Ajayi *et al.*, 2013a and 2013b; Tomar *et al.*, 2013). Tomar *et al.* (2013) found coronary atherosclerosis to be more prevalent in patients with shorter LCA lengths and therefore suggested that short LCA lengths can be a congenital predisposing factor for the development of coronary artery disease.

Conclusion

Cardiovascular diseases are the leading cause of death globally, thereby, resulting in the importance of a comprehensive understanding of the coronary arteries and their variations. A significant correlation was found in this study between a split RCA and absent LCA showing a higher prevalence of split RCA in the absence of the LCA. In addition, a significant correlation between the fetal gestational age and the lengths of the LCA and RCA indicated that there was a substantial growth of the LCA and RCA with the development of the fetal heart. With the advent of coronary angiography and cardiopulmonary bypass surgery a failure to identify the morphological characteristics of these arteries can lead to misinterpretation. Therefore, an in-depth knowledge of coronary arterial anatomy and its variations is essential.

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APPENDICES

Appendix A

DOCUMENTS RELATED TO DATA COLLECTION

Angiographic Data Sheet

ANGIOGRAM NUMBER	GENDER	ETHNICITY	LCA	LCA PATTERN	SPLIT RCA	RCA PATTERN	DOMINANCE	RCA SHAPE
8861	male	white	absent	absent bifurcation D	single	single A	right	C-shaped
8866	female	black	present	present trifurcation B	single	single A	right	C-shaped
8867	female	black	present	present bifurcation A	single	single A	co-dominant	C-shaped
8868	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8870	female	white	present	present bifurcation A	single	single A	right	C-shaped
8871	female	indian	absent	absent bifurcation D	split	split non dominant B	left	2 C-shaped
8872	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
8873	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8874	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8882	male	indian	present	present bifurcation A	single	single A	left	C-shaped
8891	male	indian	present	present trifurcation B	single	single A	left	S-shaped
8892	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8893	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
8894	female	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8896	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8909	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8915	male	black	present	present bifurcation A	single	single A	right	C-shaped
8923	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8924	female	indian	absent	absent bifurcation D	single	single A	co-dominant	S-shaped
8942	female	indian	absent	absent bifurcation D	single	single A	left	C-shaped
8943	female	white	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
8947	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8949	male	white	present	present quadrification C	single	single A	co-dominant	S-shaped
8950	female	white	present	present bifurcation A	single	single A	left	C-shaped
8951	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8952	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8962	female	indian	present	present trifurcation B	single	single A	left	C-shaped
8963	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
8966	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9635	male	indian	present	present trifurcation B	single	single A	co-dominant	C-shaped
9636	female	white	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
9637	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9638	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
9643	female	indian	present	present bifurcation A	single	single A	right	S-shaped
9644	male	indian	present	present trifurcation B	single	single A	right	S-shaped
8862	male	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
8864	female	indian	present	present trifurcation B	single	single A	right	S-shaped
8875	female	indian	present	present trifurcation B	single	single A	right	C-shaped
8876	male	black	present	present bifurcation A	single	single A	right	C-shaped
8877	male	indian	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
8878	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8881	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8884	female	indian	present	present bifurcation A	single	single A	right	C-shaped
			•	present quadrification				•
8885	male	indian	present	C	single	single A	right	S-shaped
8886	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8888	male	white	present	present trifurcation B	single	single A	right	C-shaped
8899	female	white	present	present bifurcation A	single	single A	right	C-shaped

8901	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8906	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8911	female	indian	present	present trifurcation B	single	single A	right	S-shaped
8913	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
8916	male	white	present	present bifurcation A	single	single A	right	C-shaped
0310	illale	writte	present	present quadrification	Single		ngnt	C-Shaped
8917	male	indian	present	С	split	split non dominant B	left	2 C-shaped
8919	male	white	present	present trifurcation B	single	single A	right	C-shaped
8921	male	white	present	present bifurcation A	single	single A	right	C-shaped
8922	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8926	male	indian	absent	absent trifurcation E	single	single A	right	C-shaped
8927	female	indian	present	present trifurcation B	single	single A	right	C-shaped
8928	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8929	male	white	present	present trifurcation B	single	single A	right	C-shaped
8932	male	white	present	present bifurcation A	single	single A	right	C-shaped
8933	male	indian	present	present trifurcation B	split	split non dominant B	left	2 C-shaped
8935	male	indian	present	present quadrification C	single	single A	right	C-shaped
8937	female	white	present	present bifurcation A	single	single A	right	C-shaped
8938	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8939	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
8940	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8945	female	indian	present	present trifurcation B	single	single A	right	S-shaped
8946	male							
8954	male	indian indian	present	present bifurcation A absent bifurcation D	single	single A	right left	C-shaped
			absent		single	single A		C-shaped
8955	female	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8956	male	indian	present	present bifurcation A	single	single A	left	S-shaped
8957	female	white	present	present bifurcation A	single	single A	left	C-shaped
8958	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8959	female	black	present	present trifurcation B	single	single A	right	S-shaped
8964	male	indian	present	present bifurcation A present quadrification	single	single A	co-dominant	C-shaped
8965	male	white	present	c	single	single A	right	C-shaped
8967	female	black	absent	absent trifurcation E	split	split non dominant B	left	2 C-shaped
8969	male	white	present	absent trifurcation E	single	single A	right	S-shaped
8970	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8971	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8972	male	black	present	present trifurcation B	single	single A	co-dominant	C-shaped
8973	male	white	absent	absent bifurcation D	single	single A	right	C-shaped
8974	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8976	male	white	present	present bifurcation A	single	single A	right	C-shaped
8977	male	indian	absent	absent trifurcation E	single	single A	right	C-shaped
9639	male	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
9640	male	indian	present	present trifurcation B	single	single A	right	C-shaped
7856	female	white	present	present bifurcation A	single	single A	right	C-shaped
7857	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7858	female	black	present	present bifurcation A	single	single A	right	C-shaped
7860	male	indian	present	present bifurcation A	split	split co-dominant C	co-dominant	2 C-shaped
7871	male	indian	present	present bifurcation A	single	single A	right	C-shaped
7872	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7874	male	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped
7875	female	indian	present	present bifurcation A	single	single A	right	S-shaped
7877	male	indian	present	present bifurcation A	single	single A	right	C-shaped
	maio	indian	prosont	p. soont sharoadon A	Jingio	Single /		o onapou

7879	male	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
7893	female	indian	present	present bifurcation A	single	single A	right	S-shaped
7895	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7896	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
7898	male	indian	present	present bifurcation A	single	single A	right	S-shaped
7899	female	indian	absent	absent bifurcation D	single	single A	right	C-shaped
7911	male	white	present	present bifurcation A	single	single A	right	S-shaped
7912	male	black	present	present bifurcation A	single	single A	right	C-shaped
7914	male	indian	present	present bifurcation A	single	single A	right	C-shaped
7915	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7916	male	indian	present	present bifurcation A	single	single A	right	C-shaped
7917	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7919	male	indian	present	present bifurcation A	single	single A	right	S-shaped
7920	female	indian	present	present bifurcation A	single	single A	right	S-shaped
7921	female	white	present	present bifurcation A	single	single A	right	C-shaped
7922	male	indian	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
7923	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
7924	male	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
7925	female	indian	present	present bifurcation A	single	single A	right	S-shaped
7926	female	white	present	present bifurcation A	single	single A	right	C-shaped
7927	male	indian	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
7928	female	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
7943	male	indian	present	present trifurcation B	single	single A	right	C-shaped
7948	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7950	male	indian	present	present trifurcation B	single	single A	left	S-shaped
7951	male	indian	present	present bifurcation A	single	single A	right	C-shaped
7977	male	white	present	present bifurcation A	single	single A	right	C-shaped
7979	female	indian	present	present trifurcation B	single	single A	right	C-shaped
7986	male	indian	present	present bifurcation A	split	split co-dominant C	co-dominant	2 C-shaped
7988	female	indian	present	present bifurcation A	single	single A	left	S-shaped
7989	male	indian	present	present bifurcation A	single	single A	right	S-shaped
7990	female	indian	present	present bifurcation A	single	single A	right	S-shaped
8016	female	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8019	female	indian	present	present trifurcation B	single	single A	right	C-shaped
8020	male	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
8058	female	indian	present	present bifurcation A	single	single A	left	S-shaped
8061	male	white	present	present bifurcation A	single	single A	right	C-shaped
8066	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8068	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8092	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8093	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8094	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8095	male	indian		present bifurcation A	single	single A	right	C-shaped
8104	female	indian	present present	present bifurcation A	single	single A	right	C-shaped
8110	female	indian	present	present bifurcation A	single	single A	left	C-shaped
7859	female	indian	present	present bifurcation A	single	single A	right	C-shaped
7880	female	black		present trifurcation B				C-shaped
9013		indian	present		single	single A	right left	
	female		present	present bifurcation A	single	single A		C-shaped
9014 9018	male	indian	present	present bifurcation A	single	single A	right	S-shaped
MITTR	male	white	present	present bifurcation A	single	single A	left	S-shaped
9019	male	indian	present	present bifurcation A	single	single A	right	C-shaped

9025	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9027	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
9033	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
9038	female	black	present	present bifurcation A	single	single A	co-dominant	C-shaped
9039	female	indian	present	present bifurcation A	single	single A	left	C-shaped
9046	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
9047	male	indian	absent	absent bifurcation D	single	single A	right	S-shaped
9048	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9057	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9058	female	indian	present	present trifurcation B	single	single A	right	C-shaped
9060	female	indian	present	present trifurcation B	single	single A	right	S-shaped
9064	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9066	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9067	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9068	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9077	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9078	male	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped
9079	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9080	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9088	female	black	absent	absent bifurcation D	split	split non dominant B	left	2 C-shaped
9089				present bifurcation A				C-shaped
	female	indian	present		single	single A	right	
9377	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9378	female	indian	present	present bifurcation A	single	single A	right	S-shaped
9379	female	white	present	present bifurcation A	single	single A	right	C-shaped
9380	male	indian	present	present bifurcation A	single	single A	left	C-shaped
10072	male	indian	present	present trifurcation B	single	single A	co-dominant	C-shaped
10076	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10077	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
10078	female	white	absent	absent bifurcation D	single	single A	right	C-shaped
10081	female	indian	present	present bifurcation A	single	single A	right	C-shaped
10089	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10095	male	white	present	present bifurcation A	single	single A	right	C-shaped
10096	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10097	female	white	present	present bifurcation A	single	single A	right	S-shaped
10098	male	white	present	present bifurcation A	single	single A	right	C-shaped
10103	male	white	present	present bifurcation A	single	single A	right	C-shaped
10110	female	indian	present	present bifurcation A	single	single A	left	C-shaped
10118	male	indian	present	present bifurcation A	single	single A	right	S-shaped
10119	male	indian	present	present trifurcation B	single	single A	right	S-shaped
10120	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10134	female	white	present	present bifurcation A	single	single A	right	C-shaped
10135	male	black	present	present bifurcation A	single	single A	right	S-shaped
10136	female	white	absent	absent bifurcation D	single	single A	co-dominant	S-shaped
10137	male	white	present	present trifurcation B	single	single A	right	C-shaped
10138	male	indian	present	present trifurcation B	single	single A	right	C-shaped
10140	male	indian	present	present bifurcation A	single	single A	right	S-shaped
10141	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
10149	female	indian	present	present bifurcation A	single	single A	right	C-shaped
10150	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10152	female	indian	present	present bifurcation A	single	single A	right	S-shaped
10153	male	indian	present	present bifurcation A	single	single A	right	C-shaped
10154	female	white	present	present bifurcation A	single	single A	right	C-shaped

10162	male	black	present	present bifurcation A	single	single A	co-dominant	C-shaped
10164	female	indian	present	present bifurcation A	single	single A	right	S-shaped
10165	female	indian	present	present bifurcation A	single	single A	right	S-shaped
10170	male	indian	present	present bifurcation A	single	single A	right	S-shaped
10171	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8978	male	black	present	present trifurcation B	single	single A	right	S-shaped
8981	female	indian	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
8983	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
8984	female	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped
8985	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8989	male	white	present	present trifurcation B	single	single A	co-dominant	C-shaped
8990	male	black	present	present bifurcation A	single	single A	right	C-shaped
8991	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8993	male	white	present	present trifurcation B	single	single A	right	C-shaped
8994	male	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
8996	female	indian	present	present trifurcation B	single	single A	right	C-shaped
8997	male	black	present	present trifurcation B	single	single A	left	S-shaped
8999	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9000	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
9001	female	indian	absent	absent bifurcation D	split	split non dominant B	left	2 C-shaped
9003	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9004	male	indian	present	present trifurcation B	single	single A	left	C-shaped
9005	male	black	present	present bifurcation A	single	single A	right	S-shaped
9006	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9008	male	white	present	present trifurcation B	single	single A	co-dominant	C-shaped
9009	female	white	present	present bifurcation A	single	single A	co-dominant	S-shaped
9010	male	black	present	present bifurcation A	split	split non dominant B	left	2 C-shaped
9016	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
9020	male	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
9028	male	black	present	present bifurcation A	single	single A	right	C-shaped
9031	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9032		indian		present trifurcation B	single		right	C-shaped
9034	female	indian	present	present bifurcation A	single	single A single A	right	C-shaped
9035		white	present	absent bifurcation D	Ŭ		Ŭ	S-shaped
9036	female	indian	absent present	present bifurcation A	single single	single A single A	right right	C-shaped
9037	male	indian	absent	absent bifurcation D	single	single A	left	S-shaped
9040	female	black	present	present trifurcation B	single	single A	co-dominant	C-shaped
9042	female	indian	present	present bifurcation A	single	single A	right	C-shaped
9043	female	white	present	present bifurcation A	single	single A	right	C-shaped
9052	female	indian	present	present bifurcation A	single	single A	right	S-shaped
9053	male	white	absent	absent bifurcation D	single	single A	right	C-shaped
9055	male	indian	absent	absent bifurcation D	single	single A	left	C-shaped
9056	female	white	present	present bifurcation A	single	single A	right	C-shaped
9061	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9062	male	indian		present bifurcation A	Ŭ	single A	right	C-shaped
9063	male	indian	present absent	absent trifurcation E	single single	single A	right	S-shaped
9065	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
9071	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9072	female	indian	absent	absent bifurcation D	single	single A	right	S-shaped
0074		1 Minuto	nrocont	present trifurcation B	single	single A	right	C-shaped
9074 9076	male	white indian	present present	present trifurcation B	single	single A	right	S-shaped

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9083	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
9084	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
9085	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9091	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9360	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
9361	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped	
9362	female	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped	
9363	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9364	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
9367	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9370	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped	
9371	female	white	present	present bifurcation A	single	single A	right	C-shaped	
9373	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9374	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9375	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10074	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10082	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10083	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10084	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
10086	male	white	present	present trifurcation B	single	single A	right	C-shaped	
10087	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10088	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10090	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10092	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10093	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10094	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
10100	female	indian	present	present trifurcation B	split	split non dominant B	left	2 C-shaped	
10104	male	indian	absent	absent trifurcation E	single	single A	co-dominant	C-shaped	
10105	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10106	female	indian	present	present bifurcation A	single	single A	right	S-shaped	
10107	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
10108	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped	
10111	female	indian	present	present trifurcation B	single	single A	right	S-shaped	
10112	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10113	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
10115	male	indian	absent	absent bifurcation D	single	single A	co-dominant	S-shaped	
10116	male	black	present	present trifurcation B	single	single A	right	C-shaped	
10121	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10122	male	black	present	present bifurcation A	single	single A	right	S-shaped	
10125	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
				present quadrification		Ŭ		•	
10127	male	indian	present	С	single	single A	right	S-shaped	
10128	female	indian	absent	absent bifurcation D	single	single A	left	S-shaped	
10130	female	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped	
10144	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
10145	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10147	male	indian	present	present trifurcation B	split	split non dominant B	left	2 C-shaped	
10155	female	indian	present	present bifurcation A	single	single A	right	S-shaped	
10157	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
10157	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10160	male	white	present	present bifurcation A	single	single A	co-dominant	S-shaped	
10161	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10166	female	white	present	present bifurcation A	single	single A	right	S-shaped	

10167	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
10169	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10172	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10175	female	indian	present	present bifurcation A	single	single A	right	S-shaped	
10176	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10178	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10179	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10181	female	white	present	present bifurcation A	single	single A	left	C-shaped	
10182	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10184	female	indian	absent	absent bifurcation D	single	single A	left	S-shaped	
10185	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
10186	female	indian	present	present trifurcation B	single	single A	right	S-shaped	
10187	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
10188	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10189	male	indian	absent	absent bifurcation D	single	single A	right	S-shaped	
10190	male	black	present	present bifurcation A	single	single A	left	S-shaped	
10191	female	black	present	present bifurcation A	split	split non dominant B	left	2 C-shaped	
10192	male	white	present	present trifurcation B	single	single A	co-dominant	C-shaped	
10193	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10195	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10198	female	indian	present	present trifurcation B	single	single A	co-dominant	C-shaped	
10199	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped	
10200	male	indian		present bifurcation A	single	single A	right	C-shaped	
			present						
10202	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10203	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
10204	female	indian	present	present bifurcation A	single	single A	right	S-shaped	
10206	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10208	male	white	present	present trifurcation B	single	single A	right	S-shaped	
10213	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
10214	male	white	present	present bifurcation A	single	single A	right	C-shaped	
10215	male	white	present	present bifurcation A	single	single A	right	C-shaped	
10216	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10217	female	white	present	present trifurcation B	single	single A	right	S-shaped	
10218	male	white	present	absent trifurcation E	single	single A	right	C-shaped	
10219	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
10224	male	black	present	present bifurcation A	single	single A	right	S-shaped	
9566	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9567	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9568	male	black	present	present bifurcation A	single	single A	right	S-shaped	
9573	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9574	female	white	absent	absent bifurcation D	single	single A	right	C-shaped	
9591	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9594	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9604	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9619	male	white	present	present bifurcation A	single	single A	right	C-shaped	
9628	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9631	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9633	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9558	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9564	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9565	female	indian	present	present trifurcation B	single	single A	co-dominant	C-shaped	
9569	female	indian	present	present bifurcation A	single	single A	right	C-shaped	

9570	male	indian	absent	absent bifurcation D	split	split non dominant B	left	2 C-shaped	
9575	male	white	present	present bifurcation A	single	single A	right	S-shaped	
9577	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
9578	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9581	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9584	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
9586	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9587	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
9588	male	white	present	present bifurcation A	single	single A	right	S-shaped	
9595	female	black	present	present trifurcation B	single	single A	right	C-shaped	
9597	male	indian	present	present trifurcation B	single	single A	right	S-shaped	
9598	female	indian	present	present trifurcation B	single	single A	left	C-shaped	
9602	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9603	male	indian	present	present bifurcation A	single	single A	right	C-shaped	
9605	male	indian	absent	absent bifurcation D	single	single A	left	C-shaped	
9606	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
9607	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9610	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
9612	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped	
9613	male	white	present	present bifurcation A	single	single A	right	S-shaped	
9614	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9615	female	indian	present	present trifurcation B	split	split non dominant B	left	2 C-shaped	
9616	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9623	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
9624	female	indian	present	present trifurcation B	single	single A	right	S-shaped	
9625	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
9626	female	black	present	present bifurcation A	single	single A	right	C-shaped	
9627	female	black	present	present bifurcation A	single	single A	right	C-shaped	
9629	male	indian	present	present trifurcation B	single	single A	right	C-shaped	
8723	female	white	present	present bifurcation A	single	single A	right	C-shaped	
8730	female	indian	present	present trifurcation B	single	single A	right	S-shaped	
8731	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
8732	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
8738	male	white	present	present bifurcation A	single	single A	right	C-shaped	
8740	female	indian	present	present trifurcation B	single	single A	right	C-shaped	
8741	female	black	present	present bifurcation A	single	single A	right	C-shaped	
8752	male	white	present	present bifurcation A	single	single A	co-dominant	S-shaped	
8753	female	white	present	present trifurcation B	single	single A	co-dominant	C-shaped	
8754	female	white	present	present quadrification C	single	single A	right	S-shaped	
8755	female	white	present	present trifurcation B	single	single A	co-dominant	C-shaped	
8764	female	indian	present	present bifurcation A	single	single A	right	S-shaped	
8769	male	white	present	present bifurcation A	single	single A	right	C-shaped	
8770	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped	
8771	male	white	present	present bifurcation A	single	single A	right	S-shaped	
8772	male	white	absent	absent bifurcation D	single	single A	right	C-shaped	
8773	male	white	present	present trifurcation B	single	single A	right	C-shaped	
8776	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
8783	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
8784	male	indian	present	present bifurcation A	single	single A	right	S-shaped	
8786	female	indian	present	present bifurcation A	single	single A	right	C-shaped	
8791	female	white	present	present bifurcation A	single	single A	left	C-shaped	
8792	male	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped	

8795	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8802	male	black	present	present bifurcation A	single	single A	right	S-shaped
8807	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8810	male	white	present	present bifurcation A	single	single A	right	S-shaped
8813	female	indian	present	present bifurcation A	single	single A	right	S-shaped
8814	female	white	present	present bifurcation A	single	single A	right	S-shaped
8820	female	white	present	present bifurcation A	single	single A	right	S-shaped
8821	male	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
8824	male	white	present	present bifurcation A	single	single A	right	C-shaped
8841	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8721	male	black	present	present bifurcation A	single	single A	right	C-shaped
8725	male	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
8727	female	indian	present	present trifurcation B	single	single A	right	S-shaped
8729	male	white	present	present trifurcation B	single	single A	right	C-shaped
8733	female	white	present	present bifurcation A	single	single A	right	S-shaped
8734	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8736	male	black	present	present bifurcation A	single	single A	right	S-shaped
8742	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8746	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8747	female	white	present	present bifurcation A	single	single A	right	C-shaped
8748	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8759	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8760	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8761	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8762	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8765	female	black	present	present bifurcation A	single	single A	right	S-shaped
8766	male	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped
8768	female	black	present	present bifurcation A	single	single A	right	C-shaped
8778	male	indian	present	present quadrification C	single	single A	right	S-shaped
8779	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8787	female	indian	present	present bifurcation A	single	single A right		C-shaped
8788	female	indian	present	present bifurcation A	single	single A	right	S-shaped
8790	female	white	present	present bifurcation A	single	single A	co-dominant	C-shaped
8794	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8797	female	white	present	present bifurcation A	single	single A	right	S-shaped
8798	male	white	present	present bifurcation A	single	single A	right	C-shaped
8804	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8805	female	white	present	present trifurcation B	single	single A	co-dominant	S-shaped
8808	male	indian	present	present trifurcation B	single	single A	right	C-shaped
8812	female	black	present	present bifurcation A	single	single A	right	S-shaped
8816	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8819	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8830	male	indian	present	present bifurcation A	single	single A	right	C-shaped
8832	male	black	present	present bifurcation A	single	single A	right	C-shaped
8833	male	indian	present	present bifurcation A	single	single A	right	S-shaped
8835	female	indian	present	present bifurcation A	single	single A	right	C-shaped
8842	female	indian	present	present bifurcation A	single	single A	co-dominant	C-shaped
9381	male	black	present	present bifurcation A	single	single A	right	S-shaped
9384	male	white	present	present bifurcation A	single	single A	right	C-shaped
9392	male	white	present	present bifurcation A	single	single A	left	S-shaped
9393	female	white	present	present bifurcation A	single	single A	right	C-shaped
9408	female	indian	present	present bifurcation A	single	single A	right	C-shaped

9409	female	white	present	present bifurcation A	present bifurcation A single single A		right	S-shaped
9410	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9411	male	black	absent	absent bifurcation D	absent bifurcation D single single A co-domi		co-dominant	C-shaped
9412	female	white	absent	absent bifurcation D	absent bifurcation D single single A lef		left	S-shaped
9416	male	indian	present	present bifurcation A	single	single A	co-dominant	S-shaped
9425	male	white	present	present bifurcation A	single	single A	right	C-shaped
9426	female	white	absent	absent bifurcation D	single	single A	right	C-shaped
9432	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9438	male	indian	absent	absent bifurcation D	single	single A	co-dominant	C-shaped
9439	female	white	present	present bifurcation A	single	single A	right	C-shaped
9440	male	indian	present	present bifurcation A	split	split right dominant D	right	2 C-shaped
9441	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9455	male	indian	present	present trifurcation B	single	single A	right	S-shaped
9456	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9457	male	indian	present	present trifurcation B	single	single A	right	S-shaped
9458	male	white	present	present trifurcation B	single	single A	co-dominant	S-shaped
9481	female	indian	present	present bifurcation A			right	C-shaped
9483	male	indian	present	present bifurcation A single single A		right	C-shaped	
9486	female	black	absent	absent bifurcation D			right	S-shaped
9488	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9489	female	white	present	present bifurcation A	single	single A	right	C-shaped
9385	male	indian	present	present trifurcation B	single	single A	right	C-shaped
9386	male	indian	absent	absent bifurcation D	single	single A	right	C-shaped
9387	male	indian	present	present trifurcation B	single	single A	right	S-shaped
9388	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9389	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9391	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9394	male	white	present	present bifurcation A	single	single A	right	S-shaped
9398	female	indian	present	present bifurcation A	single	single A	right	S-shaped
9399	male	indian	present	present bifurcation A	single	single A	right	C-shaped
9400	female	indian	present	present trifurcation B	single	single A	right	C-shaped
9402	male	indian	present	present bifurcation A	single	single A	right	S-shaped
9404	female	black	present	present trifurcation B	single	single A	right	C-shaped
9406	female	indian	present	present bifurcation A	single	single A	left	S-shaped
9413	female	black	present	present bifurcation A	single	single A	co-dominant	S-shaped
9415	female	white	present	present bifurcation A	single	single A	right	S-shaped
9417	female	indian	absent	absent bifurcation D	split	split non dominant B	left	2 C-shaped

Fetal Dissection Data Sheet

SPECIMEN NUMBER	AGE (mm)	AGE (WKS)	ABS/PRES LCA	LCA PATTERN	ABS/PRES SPLIT RCA	RCA PATTERN	DOMINANCE	LCA LENGTH	LCA DIAMETER	RCA LENGTH	RCA DIAMETER
516	21,18	17,18	PRESENT	А	ABSENT	А	RIGHT	2	0,6	0,6	0,3
506	30,58	22,51	PRESENT	А	ABSENT	А	RIGHT	2,9	0,7	1,2	0,5
498	26,16	20,29	PRESENT	А	ABSENT	А	RIGHT	0,7	0,3	0,6	0,4
525	25,44	19,92	PRESENT	А	ABSENT	А	RIGHT	2	0,4	0,5	0,3
493	36,99	25,73	PRESENT	А	ABSENT	А	RIGHT	2,2	0,6	1,1	0,5
540	27,5	20,96	PRESENT	А	ABSENT	А	RIGHT	0,5	0,5	1	0,6
469	20,62	17,5	PRESENT	А	ABSENT	А	RIGHT	2,1	0,3	2,2	0,3
534	26,4	20,4	PRESENT	А	ABSENT	А	RIGHT	2,6	0,6	0,9	0,2
476	24,99	19,7	PRESENT	А	ABSENT	А	RIGHT	2	0,5	1,1	0,4
499	23,44	18,92	PRESENT	А	ABSENT	А	RIGHT	1,5	0,5	2,1	0,4
543	30,02	22,23	PRESENT	А	ABSENT	А	RIGHT	2,3	0,4	0,9	0,6
536	27,09	20,76	PRESENT	А	ABSENT	А	RIGHT	1,2	0,3	0,3	0,4
467	35,61	25,04	PRESENT	А	ABSENT	А	RIGHT	2,1	0,4	1	0,4
482	28,5	21,46	PRESENT	А	ABSENT	А	RIGHT	1,8	0,7	1,9	0,6
468	20,59	17,49	PRESENT	В	ABSENT	А	RIGHT	2,1	0,4	1	0,3
462	16,48	15,42	PRESENT	А	ABSENT	А	RIGHT	1,9	0,3	0,5	0,2
471	11,93	13,13	PRESENT	А	ABSENT	А	RIGHT	0,9	0,3	1	0,3
488	20,3	17,34	PRESENT	А	ABSENT	А	RIGHT	1,2	0,6	0,8	0,3
532	20,93	17,67	PRESENT	А	ABSENT	А	RIGHT	1,2	0,2	0,7	0,3
486	24,89	19,65	PRESENT	А	ABSENT	А	RIGHT	2,6	0,7	1	0,4
490	34,36	24,41	PRESENT	В	ABSENT	А	RIGHT	2,6	0,6	2,1	0,4
495	33,88	24,17	PRESENT	В	ABSENT	А	RIGHT	2	0,4	1,6	0,5
523	35,68	25,07	PRESENT	В	ABSENT	А	RIGHT	3,4	0,6	0,4	0,4
470	24,26	19,33	PRESENT	А	ABSENT	А	RIGHT	2,8	0,3	0,6	0,3
464	20,04	17,21	PRESENT	В	ABSENT	А	RIGHT	1	0,3	0,8	0,4
496	18,71	16,54	PRESENT	А	ABSENT	А	RIGHT	2,1	0,5	0,8	0,3
475	29,52	21,99	PRESENT	А	ABSENT	А	RIGHT	1,8	0,4	1	0,5
463	32,87	23,66	PRESENT	В	ABSENT	А	RIGHT	2,1	0,5	1,4	0,5
478	34,66	24,56	PRESENT	В	ABSENT	А	RIGHT	3	0,8	1,6	0,5
480	27,23	20,83	PRESENT	А	ABSENT	А	RIGHT	1	0,4	0,3	0,3
513	15,07	14,71	PRESENT	А	ABSENT	А	RIGHT	0,3	0,3	0,3	0,1
559	27,7	21,06	PRESENT	С	ABSENT	А	RIGHT	1,9	0,5	1,3	0,3
473	39,4	26,95	PRESENT	В	ABSENT	А	RIGHT	3,5	0,8	2,1	0,6
487	39,33	26,91	PRESENT	А	ABSENT	А	RIGHT	1,9	0,6	0,7	0,4
528	21,2	17,79	PRESENT	В	ABSENT	А	RIGHT	1,6	0,5	0,3	0,4
479	22,46	18,43	PRESENT	А	ABSENT	А	RIGHT	2,3	0,5	1,2	0,4
489	30,61	22,53	PRESENT	А	ABSENT	А	RIGHT	1,6	0,4	1,1	0,4
497	19,6	16,99	PRESENT	В	ABSENT	А	RIGHT	0,7	0,4	0,3	0,2
521	20,95	17,67	PRESENT	А	ABSENT	А	RIGHT	1	1	0,6	0,5
514	19,6	16,99	PRESENT	В	ABSENT	А	RIGHT	1,7	0,5	0,6	0,3
484	19,59	16,98	PRESENT	В	ABSENT	А	RIGHT	0,8	0,4	0,5	0,2

Appendix B

DOCUMENTS RELATED TO ETHICAL APPROVAL

Ethical Approval



02 December 2015

Miss S Singh (208503216) School of Laboratory Medicine Westville Campus Sadhna_singh@live.com

BBREC reference number: BE044/15 **Protocol:** Anatomic study of the relationship between the left and the right coronary arteries. **Degree:** MMedSc

EXPEDITED APPLICATION

The Biomedical Research Ethics Committee has considered and noted your application received on 17 February 2015.

The study was provisionally approved pending appropriate responses to queries raised. Your responses dated 09 November 2015 to queries raised on 27 March 2015 have been noted and approved 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 **02 December 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 <u>http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.</u>

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 08 December 2015.

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



Professor J Tsoka-Gwegweni Chair: Biomedical Research Ethics Committee

cc: Supervisor: <u>haffajeem@ukzn.ac.za</u> cc postgrad: <u>dudhrajhp@ukzn.ac.za</u>

> Biomedical Research Ethics Committee Professor J Tsoka-Gwegweni (Chair) Westville Campus, Govan Mbeki Building Postal Address: Private Bag X54001, Durban 4000 Telephone: +27 (0) 31 260 2486 Facsimile: +27 (0) 31 260 4609 Email: <u>brec@ukzn.ac.za</u> Website: <u>http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx</u>



Founding Campuses Edgewood

Gatekeeper Letter

786

Prof EA Vanker MB ChB FRCS (Edinburgh)

Specialist Cardio-Thoracic Surgeon [Practice No: 4400569] 107 Chelmsford Road, Durban, 4001. Ph 031 2014902 (w), 031 4683860 (h)

26 November 2014

Re: Masters Thesis

Candidate: Sadhna Singh

Department: Clinical Anatomy

To: Ethics Committee UKZN

Dear Sir / Madam

I am the gatekeeper to the clinical records being used by the above candidate. I have given permission for access to my records to the Principal Investigator, Sadhna Singh.

Kind regards

Yours sincerely



Dictated but not read.

Appendix C

SCIENTIFIC PRESENTATIONS BASED ON THIS RESEARCH TO DATE

A: Manuscripts in press

 Title: Anatomic study of the morphology of the right and left coronary arteries Authors: S Singh, N Ajayi, L Lazarus, KS Satyapal Journal: Folia Morphologica (ID: 48568)

B: Manuscripts under review

1. Title: Morphologic relationship between the coronary arteries during fetal development

Authors: S Singh, N Ajayi, L Lazarus, KS Satyapal

Journal: International Journal of Morphology

C: Papers delivered at national scientific conferences

Title: Anatomic study of the morphology of the right and left coronary arteries

Authors: S Singh, N Ajayi, L Lazarus, KS Satyapal

Conference: Anatomical Society of Southern Africa (ASSA), 8 - 11 May 2016

D: Papers delivered at institutional meetings

Title: Anatomic study of the morphology of the right and left coronary arteries

Authors: S Singh, N Ajayi, L Lazarus, KS Satyapal

Institutional meeting: College of Health Science Research Symposium, University of KwaZulu-Natal, 8 – 9 September 2016