ANATOMIC AND FUNCTIONAL SIGNIFICANCE OF THE CORONARY COLLATERAL PATHWAYS IN CORONARY ARTERIAL OBSTRUCTION

by

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Submitted in fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

In the Discipline of Clinical Anatomy,

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South Africa

2014

To my wife and children

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PREFACE

The research described in this dissertation was supervised by

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Nasirudeen Ajayi

ABSTRACT

Coronary artery disease is a major cause of morbidity and mortality globally, and it is becoming an epidemic in developed as well as developing countries. In South Africa and the rest of sub-Saharan Africa, cardiovascular disease is an increasing cause of death and disability. An important cause of morbidity and mortality is the formation and rupture of atherosclerotic plaque with resultant occlusion of large and medium size arteries. In severe obstructive coronary artery disease, coronary collateral arteries serve as alternative conduits for blood flow to the myocardial tissue supplied by the obstructed vessel(s). The confirmation of the presence of coronary collateral circulation has left several questions such as the distribution, histology and anatomy of these vessels unanswered. Hence, there is still much to understand in respect of the development, potential for manipulation and the haemodynamic effects of the collateral pathways.

The most extensive description of the pathways of the coronary collateral arteries to date was reported by Levin in 1974 who recorded 22 pathways. Since this compilation, it is apparent that there has been no additional study elucidating the pathways of coronary collateral arteries in severe obstruction of the major coronary arteries. Currently, the classification of the coronary collateral arterial vasculature is based on several methods and has led to difficulty in scientific communication, as well as the assessment of their structure and function. Therefore, there is the need for a standardized systematic classification of the coronary collateral pathways.

In routine coronary angiographic reports, the precise location of atherosclerotic lesions and the presence or absence of coronary collaterals is not usually indicated. The aim of this study was to document and classify the coronary collateral pathways using angiographic imaging techniques in the presence of total obstruction of the coronary arteries; and to evaluate the importance of coronary collaterals on left ventricular function.

The study group was selected from the reviewed angiographic records of 2029 consecutive patients that had coronary catheterization performed by interventional Cardiologists for symptoms suggestive of coronary artery disease. The coronary angiograms of 286 patients (mean age: 59 ± 11 years) that met the inclusion criteria were selected for analysis from the angiograms reviewed. The sex distribution of these patients was 21.7% ($^{62}/_{286}$) females and 78.3% ($^{224}/_{286}$) males. The angiograms were obtained from the cardiac catheterization laboratories of hospitals within the private sector in the eThekwini Municipality region of KwaZulu-Natal, South Africa. Ethical approval (Ethics number BE 196/13) for the study was obtained from the University of KwaZulu- Natal Biomedical Research Ethics Committee.

A total of 329 coronary arterial total obstructions were recorded in the angiograms analyzed, and these obstructions were found in the main coronary arteries as follows: anterior interventricular branch -76 obstructions, circumflex branch -87 obstructions and right coronary artery (RCA) -166 obstructions. In the obstruction of the different segments of the main coronary arteries, a total of 115 different collateral pathways were observed as follows: anterior interventricular branch - 32, circumflex branch – 46 and RCA- 37. An algorithm is proposed in the present study for identifying and labelling the coronary collateral pathways.

The richest collateral supply was to the RCA and the least was to the circumflex branch. The present study found no significant association between patients' age and sex and the development of excellent or well-functioning collaterals. There was a significant association between the development of excellent collaterals and the proximal location of lesion in the RCA. In addition, a significant association was found between right coronary arterial dominant pattern and the development of excellent coronary collaterals in circumflex branch and RCA obstructions.

There was a significant difference ($p < 0.001$) in the mean ejection fraction (EF) calculated for the different grades of coronary collaterals. Thus, the development of excellent collaterals has a significant supportive effect on the preservation of left ventricular function as compared to patients with absent or poor collateralization. There was also a significant positive correlation between coronary collateral grades and mean EF calculated for the different collateral grades. Consequently, left ventricular myocardial perfusion was greater in patients with well-developed coronary collaterals and resulted in a better recovery of left ventricular function in the presence of myocardial ischemia or infarction. The presence of well-developed collaterals may influence decision making in the management of patients with coronary arterial obstruction. In the presence of an adequately preserved left ventricular function by coronary collaterals in asymptomatic patients, there may be no need for coronary angioplasty, stent insertion or surgical intervention.

ACKNOWLEDGEMENT

The author wishes to express his sincere gratitude to the following individuals and departments for their assistance in the preparation of this dissertation:

- **My parents**, **brothers and sisters** for their love, support and encouragement
- **Professor KS Satyapal** and **Professor EA Vanker** for their inspiration, assistance, supervision and guidance
- **University of Kwa-Zulu Natal** and the **Discipline of Clinical Anatomy** for the academic support
- The cardiac catheterization Laboratories in the private hospitals especially the staff of **Entabeni Hospital Catheterization Laboratory,** for their time and support in order to accomplish this work
- The **Interventional Cardiologists** for their time and support
- **Mr P Mohanllal** and **Mr S Gounden,** Discipline of Clinical Anatomy for their technical assistance with the practical material and their help and support in so many ways
- **Mr Domnic Marera** for his support and assistance during this work
- **Mr Boikhutso Tlou** for his kind assistance in the statistical evaluation
- **My family** and **friends** for their encouragement and love
- **Ms Lelika Lazarus** for her encouragement, advice, support and assistance in all aspects of this work
- My wife- **Ruqoyyah**, my children- **Sakeenah, Summayyah, Muhammad** and **Sofiyyah** for their love, understanding, patience, support and encouragement

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LIST OF ABBREVIATIONS

ABBREVIATION	INTERPRETATION
AIB	Anterior interventricular branch
Ang	Angiopoietin
AV	Atrioventricular
AVCx	Atrioventricular branch of circumflex
AVG	Atrioventricular groove
AVN	Atrioventricular node
BARI	Bypass Angioplasty Revascularization Investigation
CASS	Coronary Artery Surgery Study
CB	Conus branch
CL	Collagen
CTO	Chronic total occlusion
Cx	Circumflex branch
D	Diagonal artery
EF	Ejection Fraction
EL	Elastin
Fib	Fibrillin
IV	Interventricular
LA	Left atrium
LAC	left atrial circumflex
LAD	Left anterior descending
LAO	Left anterior oblique
LCA	Left coronary artery
LM	Left marginal
LV	Left ventricle

ABBREVIATION	INTERPRETATION
LVEF	Left ventricular ejection fraction
MB	Median branch
MCE	Myocardial contrast echocardiography
MI	Myocardial infarction
MØ	Macrophage
RA	Right atrial
RVB	Right ventricular branch
PA	Pulmonary Artery
PIB	Posterior interventricular branch
RA	Right auricle
RAO	Right anterior oblique
RCA	Right coronary artery
RMA	Right marginal artery
RPL	Right postero-lateral
SA	Sinu-atrial
S	Septal
SMC	Smooth muscle cell
TIMI	Thrombolysis in Myocardial Infarction
VEGF	Vascular endothelial growth factor
VEGFR	Vascular endothelial growth factor receptor

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

Coronary artery disease is a major cause of morbidity and mortality globally, and it is becoming an epidemic in developed as well as developing countries (Guha *et al*., 2012). In South Africa and the rest of sub-Saharan Africa, cardiovascular disease is an increasing cause of death and disability (Reddy and Yusuf, 1998; Mbewu, 2009). In addition, there is a rapid increase in the number of patients with coronary arterial or peripheral vascular disease (Royen *et al*., 2000). The main cause of myocardial infarction (MI) is coronary artery atherosclerosis, which results from an excessive, inflammatory, fibro-proliferative reaction in the arterial wall endothelial lining and smooth muscles (Ross, 1981). An important cause of morbidity and mortality is the formation and rupture of atherosclerotic plaque with resultant occlusion of large and medium size arteries (Myers *et al*., 2001).

In obstructive coronary artery disease, coronary collateral arteries serve as alternative conduits for blood flow to the myocardial tissue supplied by the obstructed vessel(s) (Berry *et al*., 2007). Therefore, they are a "natural coronary arterial bypass" to the region supplied by the obstructed vessels (Koerselman *et al*., 2003; Turgut *et al*., 2009; Meier *et al*., 2012). The coronary collaterals are anastomotic connections between portions of same or different coronary arteries without an intervening capillary bed (Koerselman *et al*., 2003). The confirmation of the presence of coronary collateral circulation has left several questions such as the distribution, histology and anatomy of these vessels unanswered (Loukas *et al*., 2009a). The complex mechanism responsible for coronary

collateral development is still not properly understood (Sun *et al.*, 2013). Hence, there is still much to understand in respect of the development, potential for manipulation and the haemodynamic effects of the collateral pathways (Ladwiniec and Hoye, 2013).

The most extensive description of the pathways of the coronary collateral arteries to date was reported by Levin in 1974. Some of the collateral arteries in his study were similar, being mentioned more than once, because they were identified in patients with different coronary arterial obstruction. Since this compilation of the collateral arteries, it is apparent that there has been no additional study elucidating the pathways of coronary collateral arteries in severe obstruction of the major coronary arteries. Therefore, the common patterns and the possible variations of these coronary collateral arteries are still not well-outlined (Loukas *et al*., 2009a).

Currently, the classification of the coronary collateral arterial vasculature is based on several methods and has led to difficulty in scientific communication, as well as the assessment of their structure and function (Loukas *et al*., 2009a). Due to the anatomic and clinical relevance of these pathways, Levin *et al*., (1973) stressed that adequate knowledge of these pathways goes beyond an ordinary academic exercise. As a consequence of the lack of standardization in the system of classification of the coronary collateral arteries, there is confusing data about their presence and clinical relevance (Loukas *et al*., 2009a). Therefore, there is the need for a standardized systematic classification of the coronary collateral pathways in coronary artery disease.

The precise description of coronary vascular anatomy, location and severity of atherosclerotic lesions determines the clinical importance of the myocardial region 'at risk' in coronary artery disease (Alderman and Stadius, 1992). In addition, reproducible interpretation and consistency in the terminologies used during diagnostic and therapeutic angiographic procedures are essential in the management of patients with coronary artery disease (Alderman and Stadius, 1992). A comprehensive appreciation of the anatomy of the coronary arterial system and the coronary collateral pathways is crucial in the management of cardiac patients. With the extensive use of radiographic images as diagnostic tool and the development of non-invasive treatments, a detailed knowledge of the normal coronary anatomy, its variations and/or anomalies and collateral pathways is a necessity (Vilallonga, 2003). Are coronary collaterals channels underestimated in clinical practice? Should the presence of the coronary collaterals influence clinical decision making in patients with coronary arterial obstruction? These are some of the questions that the present study hopes to examine.

Aim

The aim of this study was to document and classify the coronary collateral pathways using angiographic imaging techniques in the presence of total obstruction of the coronary arteries; and to evaluate the importance of coronary collaterals on left ventricular function. This information is important in order to establish a standardized anatomic classification system for the coronary collateral pathways and determine the precise role of these pathways in preserving ventricular function in cases of total coronary artery obstruction. This study will extend the knowledge in the fields of

anatomy, angiography and coronary arterial surgery. In particular, it will provide information regarding the influence of age and sex on coronary collateral development in a South African population that is hitherto unavailable.

Research objectives

The objectives of this study are to:

1. Document the coronary collateral pathways and their direction of flow in the presence of total obstruction of the major coronary arteries [i.e. the right coronary artery (RCA), the left coronary artery (LCA), and their branches such as the anterior interventricular branch and the circumflex branch]
2. Determine the influence of age and sex on coronary collateral arterial development in total coronary arterial obstruction
3. Determine the influence of the location of coronary arterial obstruction on the development of functional coronary collateral pathways in the presence of severe coronary artery disease
4. Determine the morphologic factors that promote or affect the development of coronary collaterals such as the branching patterns of the LCA, closeness of the obstructed vessels to other vessels and coronary arterial dominance
5. Evaluate the effect of coronary artery collaterals on ventricular function in the presence of total coronary artery obstruction

CHAPTER 2

REVIEW OF LITERATURE

2.1 ANATOMY OF THE CORONARY ARTERIES

2.1.1 HISTORICAL PERSPECTIVE

The study of the coronary vasculature dates back to the 15th century when Leonardo Da Vinci (1452-1519) depicted in his drawings, the heart and the circulatory apparatus. He stated that "the coronary vessels nourish the heart" (Figure 1) (Baumgartner, 1932).

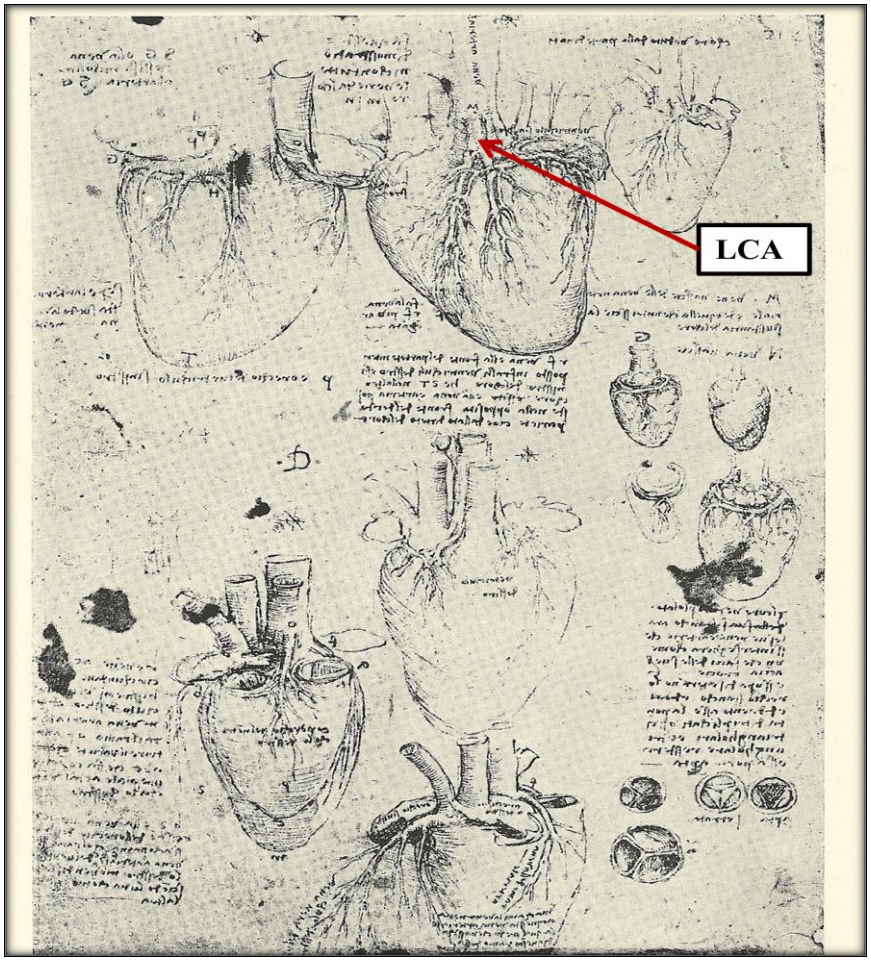

Figure 1: *Early sketches of the coronary arteries by Leonardo Da Vinci (Adapted from Baumgartner, 1932)*

Key: **LCA** –Left coronary artery

Shortly after Da Vinci's description of the heart, there was the treatise on the heart and the coronary vasculature written by Raymond Vieussens (1641-1715). He gave the first correct description of the coronary vessels and the valve in the large coronary vein (Figures 2 and 3) (Major, 1932).

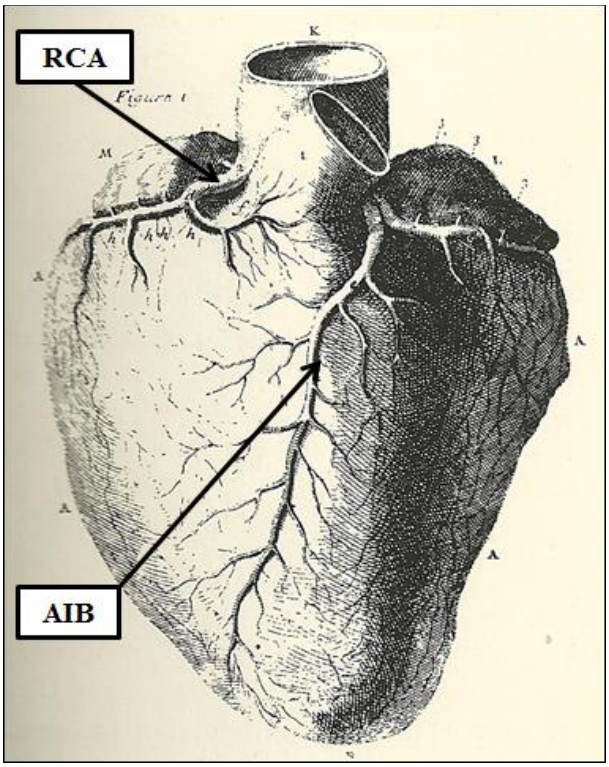

Figure 2: *Anterior view of the heart illustrating the coronary vessels by* ***Raymond Vieussens*** *(Adapted from Major, 1932)*

Key: **RCA** –Right coronary artery, **AIB-** anterior interventricular branch

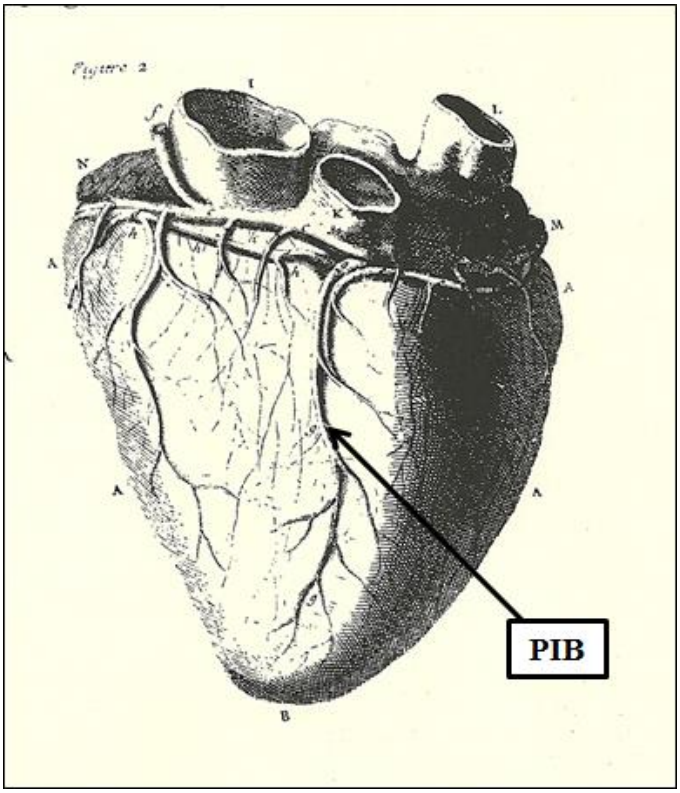

Figure 3: *Posterior view of the heart illustrating the coronary vessels by Raymond Vieussens (Adapted from Major, 1932)*

Key: **PIB**- posterior interventricular branch

In the centuries that followed, the study of coronary vasculature progressed and in the 17th century, Lower (1649) described the anastomosis between the coronary arteries (Vilallonga, 2003). In the middle of the 20th century, especially from the 1960s there was an increase in the number of investigations on coronary vascular anatomy (Fazliogullari *et al.,* 2010). Therefore, in the last four decades, several studies were conducted evaluating the embryology of the coronary arteries (Bogers *et al*., 1989; Bernanke and Velkey, 2002; Ando *et al*., 2004; Kattan *et al*., 2004), coronary arterial tree anatomy (Muriago *et al*., 1997; Reig and Petit, 2004), variations in coronary arterial vasculature

(Vilallonga, 2003; Fazliogullari *et al.*, 2010), coronary collateral pathways (Levin, 1974; Rentrop *et al*., 1985; Werner *et al*., 2003) and the effect of coronary arterial anatomy on the etiology and evolution of coronary arterial diseases (Saltissi *et al*., 1979 Dvir *et al*., 2003).

2.1.2 NOMENCLATURE OF CORONARY ARTERIES

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

Table 1: *Coronary artery nomenclature*

VARIOUS TERMINOLOGIES	CURRENT STUDY
Left main coronary artery (LMCA)/ Left main stem (LMS)/ Left coronary artery (LCA)	Left coronary artery (LCA)
Left anterior descending (LAD) artery/ Anterior interventricular branch	Anterior interventricular branch
Left circumflex branch (LCircumflex)/ Circumflex branch	Circumflex branch
Obtuse marginal (OM) artery/ Left marginal (LM) artery	Left marginal (LM) artery
Diagonal artery	Diagonal artery
Septal perforators/ Septal branches	Septal branches
Ramus medianus / Ramus intermedius, Median branch	Median branch
Left posterolateral branch	Left posterolateral branch
Right coronary artery (RCA)	Right coronary artery (RCA)
Posterior descending artery (PDA)/ Posterior interventricular artery (PIB)	Posterior interventricular artery (PIB)
Sinu-atrial branch	Sinu-atrial branch
Conal branch	Conal branch
Right ventricular branch	Right ventricular branch
Acute marginal (AM) branch/ Right marginal artery (RMA)	Right marginal artery (RMA)
Atrioventricular (AV) node branch	Atrioventricular (AV) node branch
Right posterolateral branch	Right posterolateral branch

2.1.3 THE ORIGIN OF THE CORONARY ARTERIES FROM THE AORTA

The early segment of the aortic root is occupied by the aortic sinuses, which consist of the leaflets of the aortic valve and the bulbous sinus (Fiss, 2007) and it is confined distally by the sinutubular junction (Vlodaver *et al*., 1975) (Figures 4).

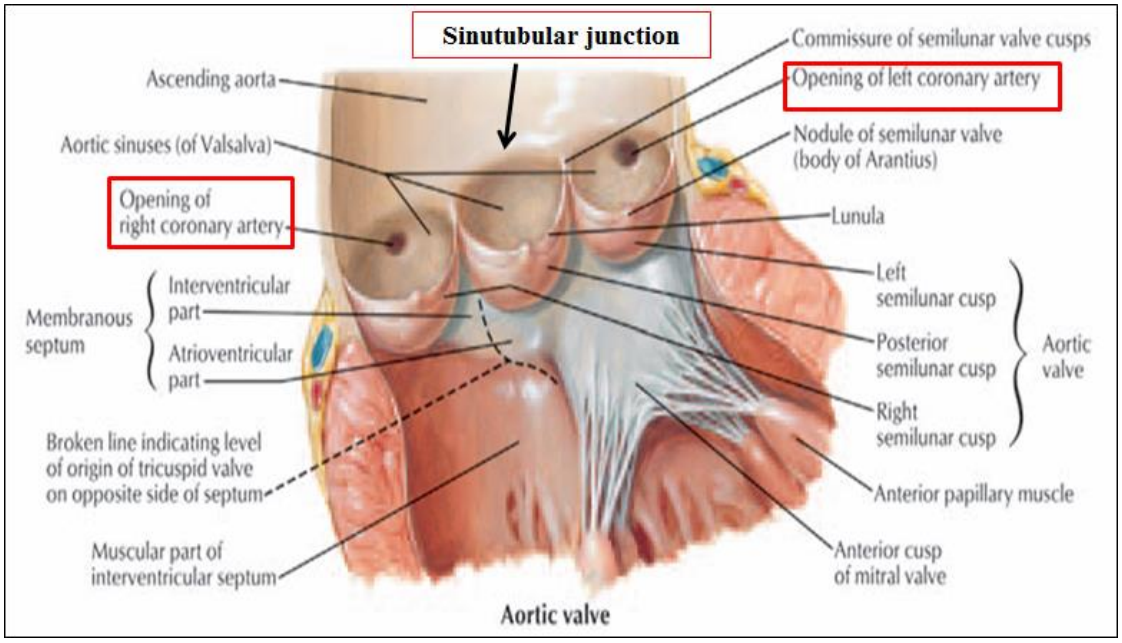

Figure 4*: The aortic root dissected open showing the aortic valve cusps and the ostia of the coronary arteries (Adapted from Fiss, 2007)*

The major coronary arteries which are the RCA and LCA arise from the anterior and left posterior sinuses of the ascending aorta (Standring *et al*., 2008). These two sinuses are adjacent to the pulmonary trunk (Loukas *et al*., 2009b). There is great variability in the origin of these arteries in relation to the sinutubular junction and the region of apposition between the aortic valvular leaflets (Muriago *et al*., 1997). The origin of the coronary artery within 1 cm of the sinutubular junction is considered variations of normal, whereas

origins greater than 1 cm relative to the junction are regarded as ectopic origins (Loukas *et al*., 2009b). In relation to the origin of the major coronary arteries, the aortic sinuses can be termed the right coronary, left coronary and non-coronary sinuses, respectively. It is rare for any of the vessels to originate from the sinus farthest from the pulmonary trunk (Loukas *et al.*, 2009b) (Figure 5).

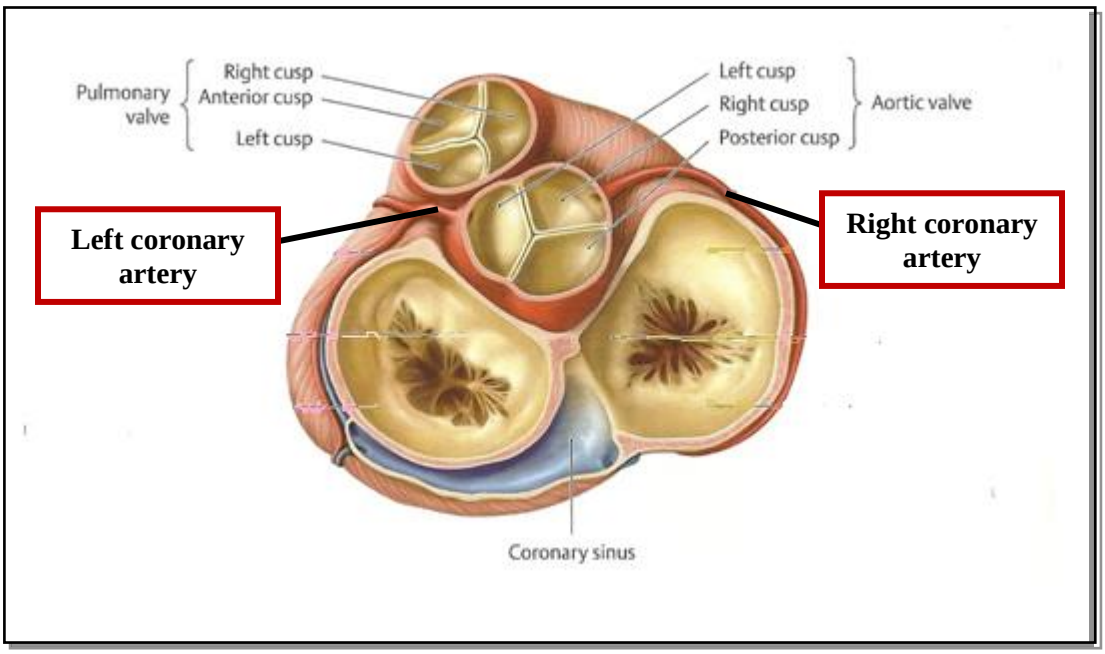

Figure 5*: Superior view of the heart (with both atria removed) showing origins of the right and left coronary arteries from right and left aortic sinuses.*
(Adapted from Gilroy et al., 2008)

The coronary arteries and their major branches are distributed over the surface of the heart, lying within the subepicardial connective tissue (Snell, 2008) (Figure 6). The coronary arteries only dip into the myocardium at or near their termination (Edwards *et al*., 1956), but sometimes a segment of the epicardial artery can have an intramural

course (Ge *et al.*, 1994) or a band of cardiac muscle crossing over the coronary artery (Bandyopadhyay *et al.*, 2010). This shift from the usual anatomy is commonly described as a "myocardial bridge" (Soran *et al*., 2000).

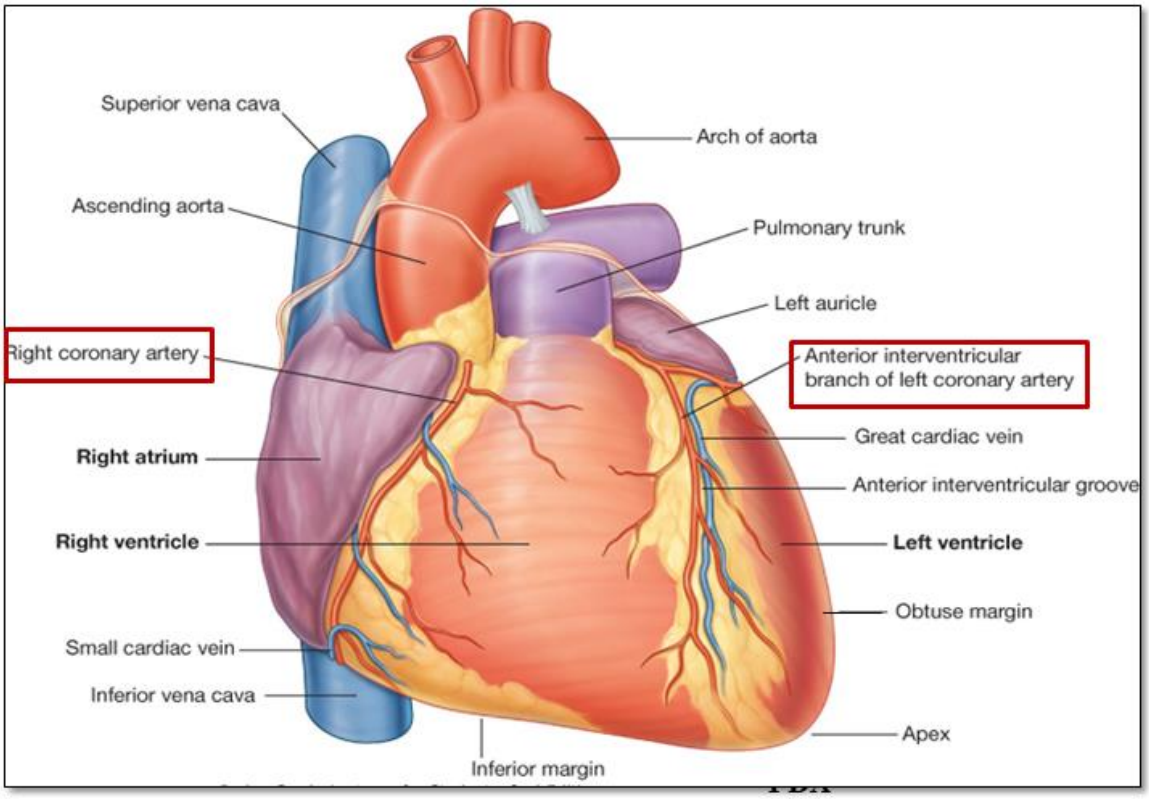

***Figure 6**: Anterior view of the heart showing the subepicardial course of major coronary arteries (Adapted from Drake et al., 2009)*

2.1.4 MORPHOLOGY OF THE CORONARY ARTERIES

2.1.4.1 THE LEFT CORONARY ARTERY

At the atrioventricular groove, the LCA divides mostly into two [anterior interventricular branch and circumflex branch] or (sometimes) into three (with an "additional" branch) (Standring *et al*., 2008) or four branches (with two "additional" branches) (Ajayi *et al*., 2013a) (Figures 7 and 8). The incidence of the division of the LCA into more than two branches in the literature reviewed is 14-60% and 2-10% for three and four branches, respectively. The division of the LCA into up to five branches has also been reported in the literature (Kalpana, 2003; Bhimalli *et al*., 2011).

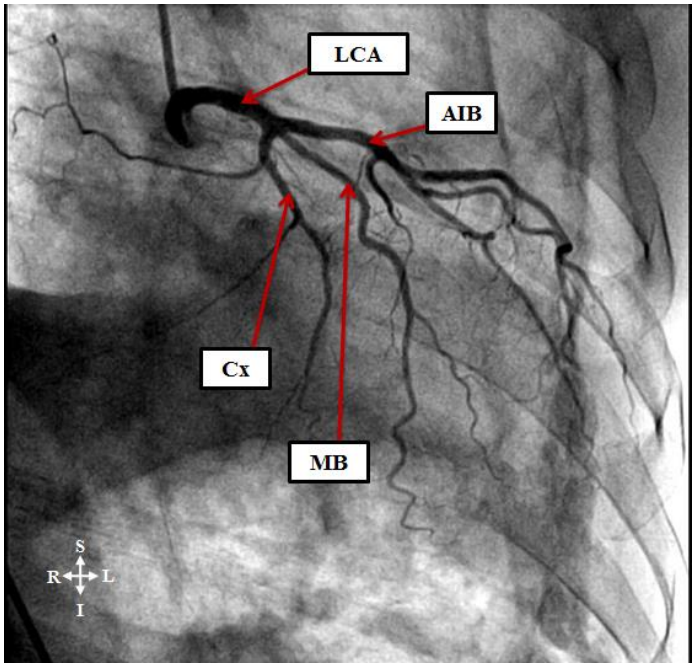

Figure 7*: Coronary angiogram in the RAO projection showing trifurcation of the LCA into anterior interventricular branch, circumflex branch and a median branch of LCA (Adapted from Ajayi et al., 2013a)*

Key: **LCA** - Left coronary artery, **Cx** - Circumflex branch, **AIB**- anterior interventricular branch, **MB** – Median branch

However, in the literature reviewed, this "additional" branch has been referred to as the "ramus diagonalis" (Baptista *et al*., 1991); "median (or intermedian)" branch (Reig and Petit, 2004 and Fazliogullari *et al*, 2010) and "diagonal branch" (Ortale *et al*., 2005). In clinical textbooks, these "additional" terminal branches are named the "ramus medianus artery" (Townsend *et al.*, 2004) or the "ramus intermedius branch" (Topol *et al*., 2002). In this dissertation, these additional branches will be represented by the term median branch. The absence of the LCA has been reported with the anterior interventricular branch and circumflex branch originating directly from the left aortic sinus (Cankaya *et al*., 2009; Ajayi *et al*., 2014).

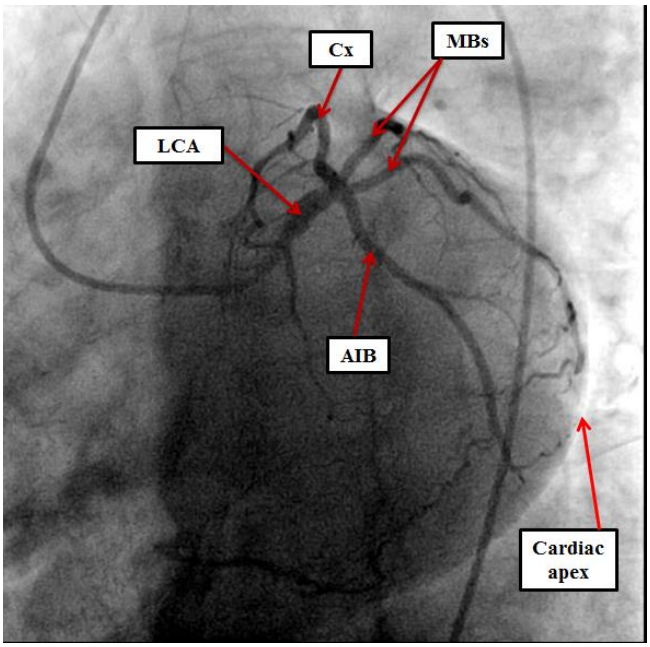

Figure 8: *Coronary angiogram in the LAO projection (caudal view) showing the quadrifurcation of the LCA into anterior interventricular branch, circumflex branch (Cx) and two median branches (MBs)*

(Adapted from Ajayi et al., 2013a)

Key: **LCA -** Left coronary artery, **Cx -** Circumflex branch, **AIB-** anterior interventricular branch, **MB** – Median branch

2.1.4.2 THE RIGHT CORONARY ARTERY

After leaving the right coronary sinus, the RCA encircles the vestibule of the tricuspid valve and continues posteriorly to the region where the interventricular and inter-atrial grooves meet - a point referred to as the "crux" of the heart (Standring *et al*., 2008; Moore *et al*., 2010). The RCA gives off the right conus artery (as its first branch) and usually terminates a little to the left of the crux by anastomosing with the circumflex branch in about 60% of individuals (Standring *et al*., 2008; Moore *et al*., 2010). The RCA also gives rise to the sinu-atrial (SA) node and the atrioventricular (AV) node arteries (Fiss, 2007) and the right marginal artery. In about 90% of the population, having reached the crux, the RCA gives rise to the posterior interventricular branch.

2.1.4.3 CORONARY ARTERIAL DOMINANCE

There is variation in the blood supply to the diaphragmatic surface of both ventricles. The origin, size, and distribution of the posterior interventricular branch are variable (Snell, 2008). The posterior interventricular branch supplies a variable portion of the diaphragmatic wall of the heart (Loukas et al., 2009b). This arrangement is called right coronary arterial dominance (Snell, 2008; Standring *et al*., 2008) (Figure 9).

In left coronary arterial dominance, the posterior interventricular branch is from the circumflex branch of the LCA. Therefore, the arterial supply to the anterior and posterior walls is from the LCA, and the occlusion of this vessel may cause severe complications of myocardial infarction.

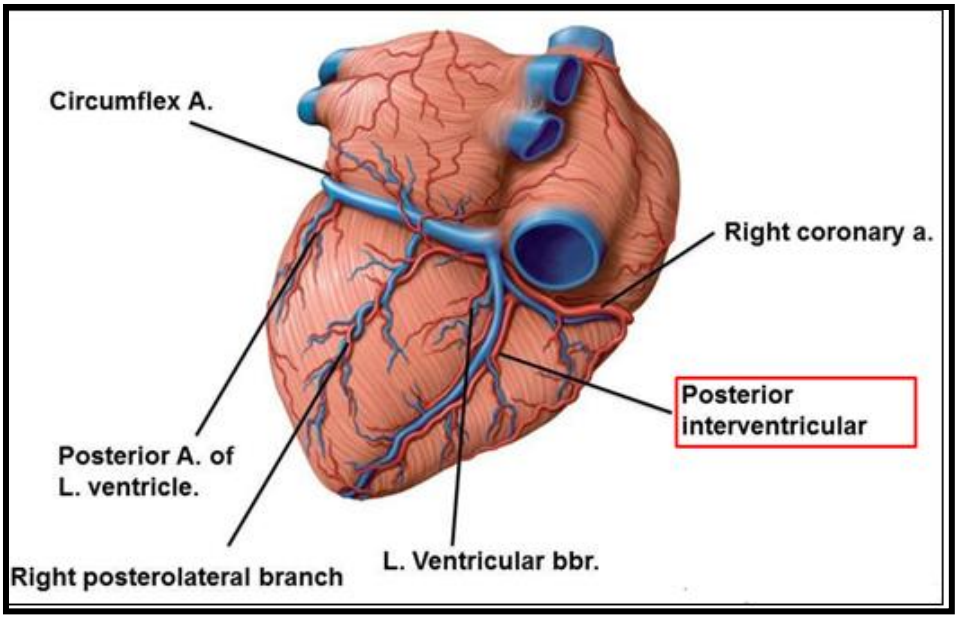

***Figure 9**: Posterior view of the heart showing the posterior interventricular branch in right coronary dominance. (Adapted from Gilroy et al., 2008)*

2.2 ANGIOGRAPHIC ANATOMY OF THE CORONARY ARTERIES

Coronary angiography is a significant diagnostic procedure in the assessment of the magnitude and severity of coronary artery disease (Alderman and Stadius, 1992). Analyzing coronary arteries in the clinical environment requires an appreciation of the anatomy of the coronary arteries as exhibited on an angiogram. An adequate understanding of the arterial patterns of the coronary arteries from this point of view is essential for an accurate clinical interpretation. The introduction of newer treatment modalities such as thrombolysis and angioplasty in the management of coronary artery disease patients requires comprehensive consideration of coronary angiographic features that might predict the possible outcome (Alderman and Stadius, 1992).

2.2.1 OBSERVATION OF THE CORONARY ARTERIES IN THE LEFT LATERAL PROJECTION

Left Coronary Artery

In this projection, the LCA is seen virtually end-on, so it is significantly fore-shortened and no conclusion may be drawn about it. The anterior interventricular branch and circumflex branch are clearly spread out in this view. The anterior interventricular branch courses anteriorly, giving off septal branches or septal perforators that appear to move away from the camera and diagonal branches that appear to move toward the camera. Characteristically, the anterior interventricular branch may be identified in this view as it is the most anterior vessel (Figures 10 and 11). The circumflex branch runs posteriorly in a curve that bulges anteriorly and has variable termination, but at the crux of the heart, it is seen giving off a branch to the AV node (Raphael *et al*., 1980). The branches that arise from it, project laterally onto the free ventricular wall. Often, these left marginal arteries

may distort the view of the circumflex branch. In this instance, the circumflex branch may be recognized by its tighter curve and by its pattern of termination.

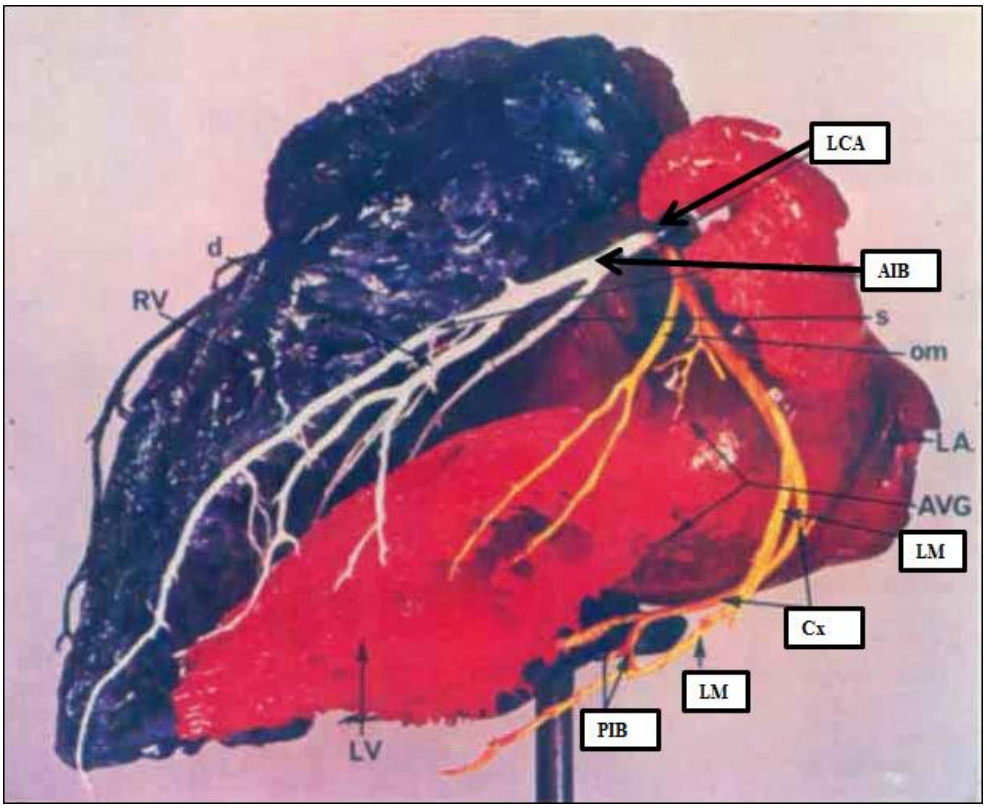

***Figure 10**: Cast of the heart showing the LCA and branches in the left lateral view (Adapted from Raphael et al., 1980)*

Key: **LCA**- left coronary artery, **AIB**- anterior interventricular branch, **Cx**- circumflex branch, **PIB**- posterior interventricular branch, **LM**- left marginal, **D**- diagonal, **RV**- right ventricle, **S**- septal, **LV**- left ventricle, **AVG**- atrioventricular groove, **LA**- left atrium

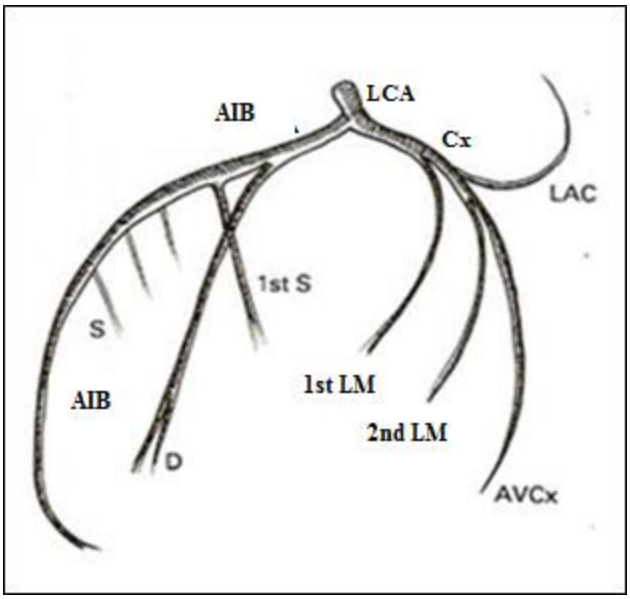

***Figure 11**: Schematic diagram of the LCA and branches in the left lateral view (Adapted from Gaze, 2013)*

Key: **LCA**- left coronary artery, **AIB**- anterior interventricular branch, **Cx**- circumflex branch, **LM**- left marginal, **D**- diagonal, **AVCx**- atrioventricular branch of circumflex, **S**- septal, **LAC**- left atrial circumflex

2.2.2 OBSERVATION OF THE CORONARY ARTERIES IN THE LEFT ANTERIOR OBLIQUE (LAO) VIEW

a) Left Coronary Artery

The proximal part of the anterior interventricular branch is very foreshortened until after the first septal and diagonal branches have been given off. This projection is not optimal for viewing the anterior interventricular branch and circumflex, but it is useful in distinguishing the diagonal branches from the septal branches of the anterior interventricular branch (Figures 12 and 13). The septal branches run to the left (and backwards) to enter the interventricular septum, while the diagonal branches pass to the right (and forwards) to supply the left ventricular free wall (Raphael *et al*., 1980). The

LAO-caudal angulation ("spider view") shows the angle of division of the LCA better, however, the LCA length is shortened in this view.

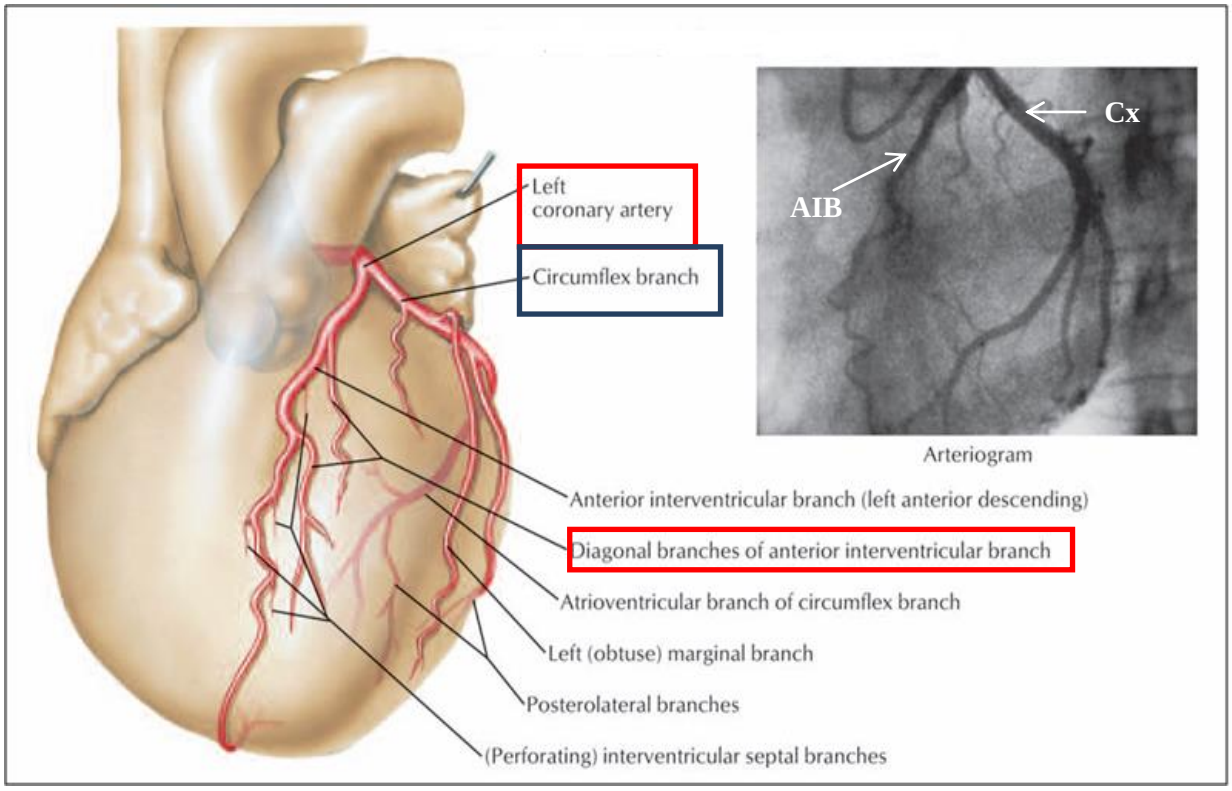

***Figure 12**: LCA and branches in the LAO view (Adapted from Netter, 2003)*

Key: **AIB-** anterior interventricular branch, **Cx-** circumflex branch.

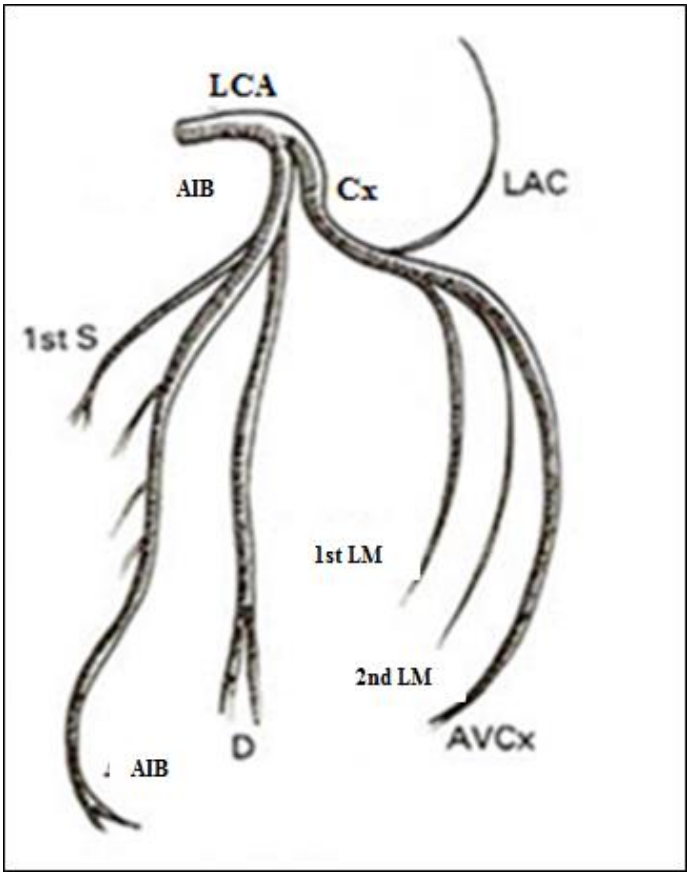

***Figure 13**: Schematic diagram of the LCA and branches in the left anterior oblique (LAO) view (Adapted from Gaze, 2013)*

Key: **LCA**- left coronary artery, **AIB**- anterior interventricular branch, **Cx**- circumflex branch, **LM**- left marginal, **D**- diagonal, **AVCx**- atrioventricular branch of circumflex, **S**- septal, **LAC**- left atrial circumflex

b) Right Coronary Artery

Raphael *et al*. (1980) described the LAO view of the RCA as follows: In this projection, the ostium and proximal part of the RCA are well appreciated. The RCA passes in the right atrioventricular groove (AVG) descending on the right heart border onto the undersurface of the heart. It makes an inverted 'U' loop marking the position of the crux with the artery to the AV node originating from its apex. Sometimes, it continues in the

AVG beyond the crux and terminates as a large posterolateral left ventricular artery. In this view, fore-shortened right ventricular branches may be recognized as they pass to the left towards the camera. The atrial artery and its SA node branches would pass to the right, as it is going backwards to supply the left atrium. There is shortening of the small right marginal artery and the right ventricular branch as it courses towards the camera to supply the acute margin*"* (Figures 14 and 15).

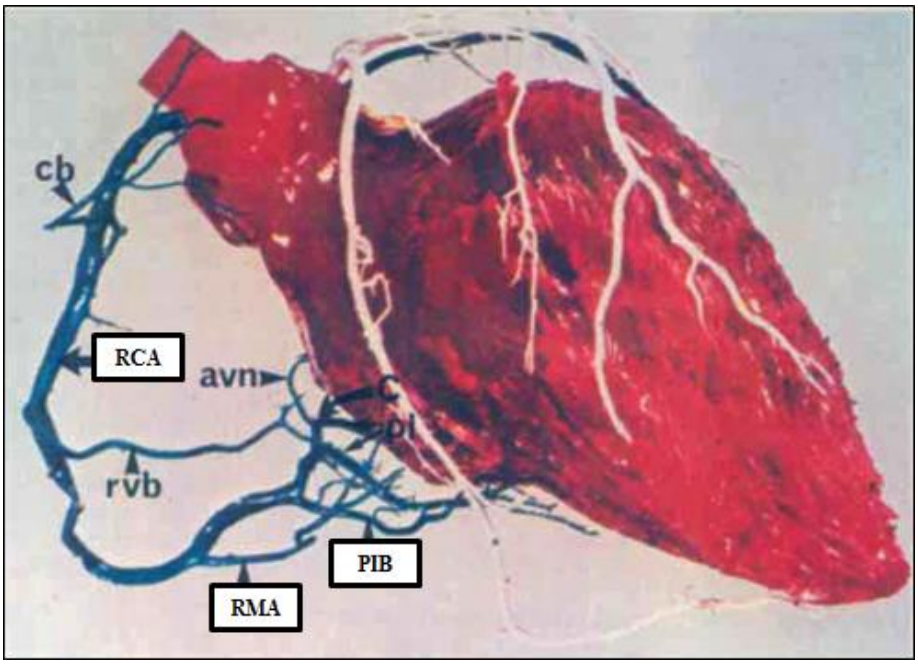

Figure 14*: Cast of the heart showing the RCA and branches in the left anterior oblique (LAO) view (Adapted from Raphael et al., 1980)*

Key: **RCA**- right coronary artery, **RMA**- right marginal artery, **PIB**- posterior interventricular branch, **CB**- conus branch, **RVB**- right ventricular branch, **S**- septal, **AVN**- atrioventricluar node branch

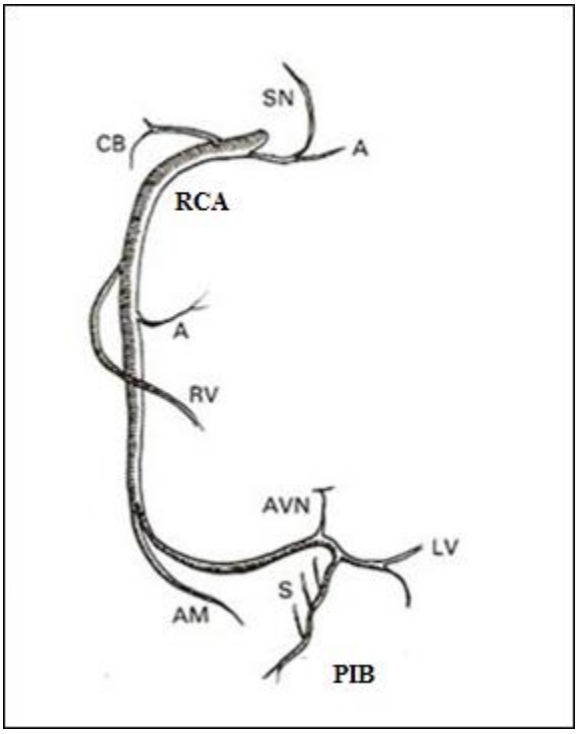

***Figure 15**: Schematic diagram of the RCA and branches in the left anterior oblique (LAO) view (Adapted from Gaze, 2013)*

Key: **RCA**- right coronary artery, **A**- atrial branch, **AM**- acute marginal (**RMA**- right marginal artery), **PIB**- posterior interventricular branch, **CB**- conus branch, **RV**- right ventricular branch, **S**- septal, **AVN**- atrioventricluar node branch, **LV**- left ventricular branch, **SN**- sinoatrial node branch

2.2.3 OBSERVATION OF THE CORONARY ARTERIES IN THE RIGHT ANTERIOR OBLIQUE (RAO) VIEW

a) Left Coronary Artery

The LCA may be identified in this projection using the points of origin of the anterior interventricular branch and circumflex branch. The circumflex branch has a characteristic straight appearance in this view. The circumflex branch is seen clearly in this view as it

continues around the atrioventricular groove and the anterior interventricular branch is most clearly observed in this projection. A certain degree of overlapping of the diagonal branches by the anterior interventricular branch may result when these diagonal branches lie in a similar position. This confusion may be limited by applying a cranio-caudal angulation in this view and the origin of the diagonals may be identified. The anterior interventricular branch may be characterized in this position and further recognized by the straight septal branches that arise from it, and by the curved pathway it takes to reach the inferior surface of the heart (Figures 16 and 17).

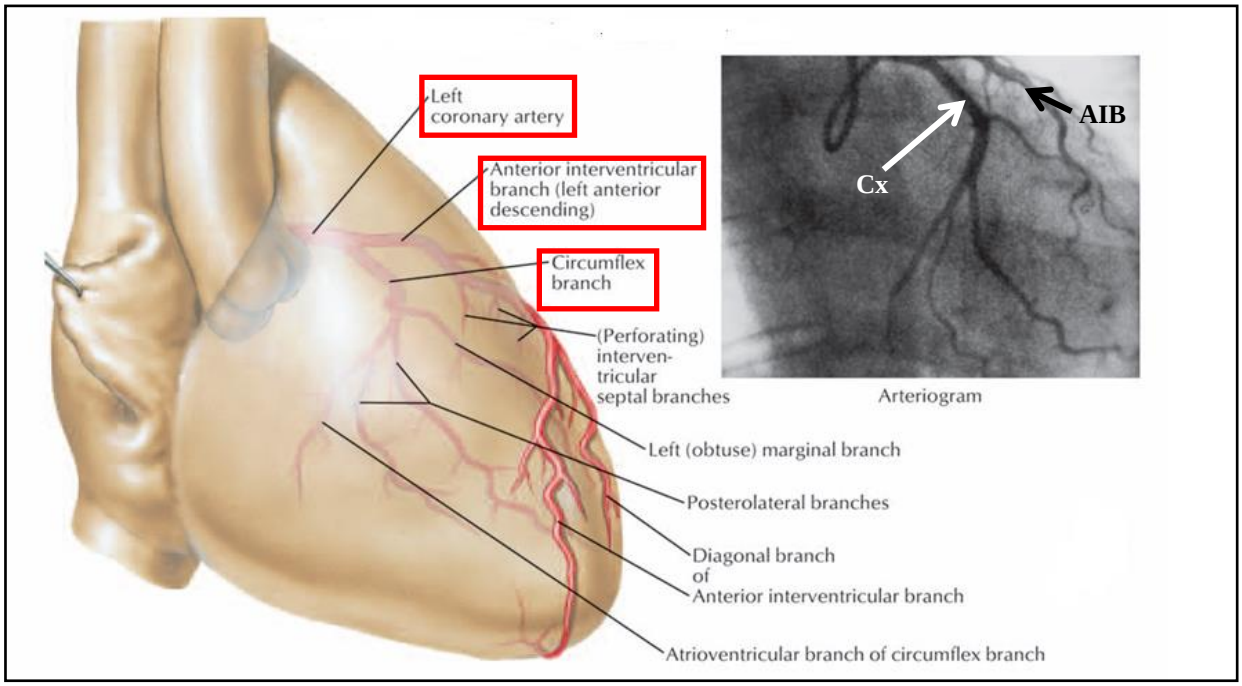

***Figure 16**: LCA and branches in the right anterior oblique (RAO) view (Adapted from Netter, 2003)*

Key: **AIB**- anterior interventricular branch, **Cx**- circumflex branch.

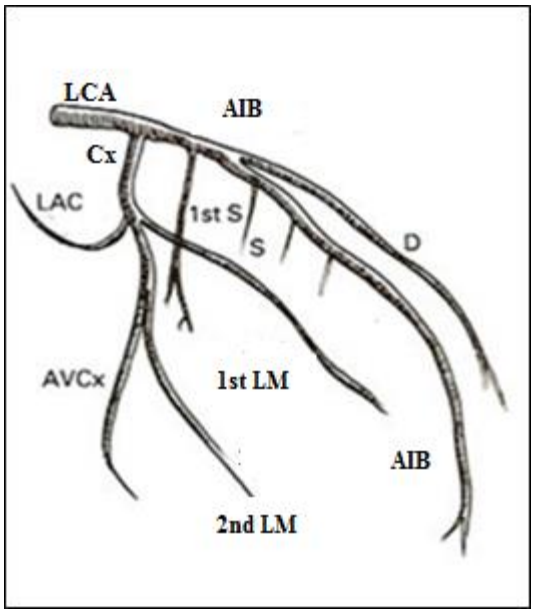

Figure 17*: Schematic diagram of the LCA and branches in the right anterior oblique (RAO) view (Adapted from Gaze, 2013)*

Key: **LCA**- left coronary artery, **AIB**- anterior interventricular branch, **Cx**- circumflex branch, **LM**- left marginal, **D**- diagonal, **AVCx**- atrioventricular branch of circumflex, **S**- septal, **LAC**- left atrial circumflex

b) Right Coronary Artery

The RCA is seen in a good profile as it descends in the right AVG over the right side of the heart. It then turns in the AVG on the undersurface of the heart and recedes from the camera, becoming distorted by foreshortening. The 'U' loop of the crux with the AV node artery rising from its apex into the septum is recognized, but no detail is seen because of overlapping. In this view, the right marginal branch, the posterior interventricular branch and posterolateral left ventricular branches are all also seen in good profile as they run in, or parallel to the posterior interventricular groove which is

virtually parallel to the film. The posterior interventricular branch may be identified by its septal branches (Raphael *et al*., 1980) (Figures 18 and 19).

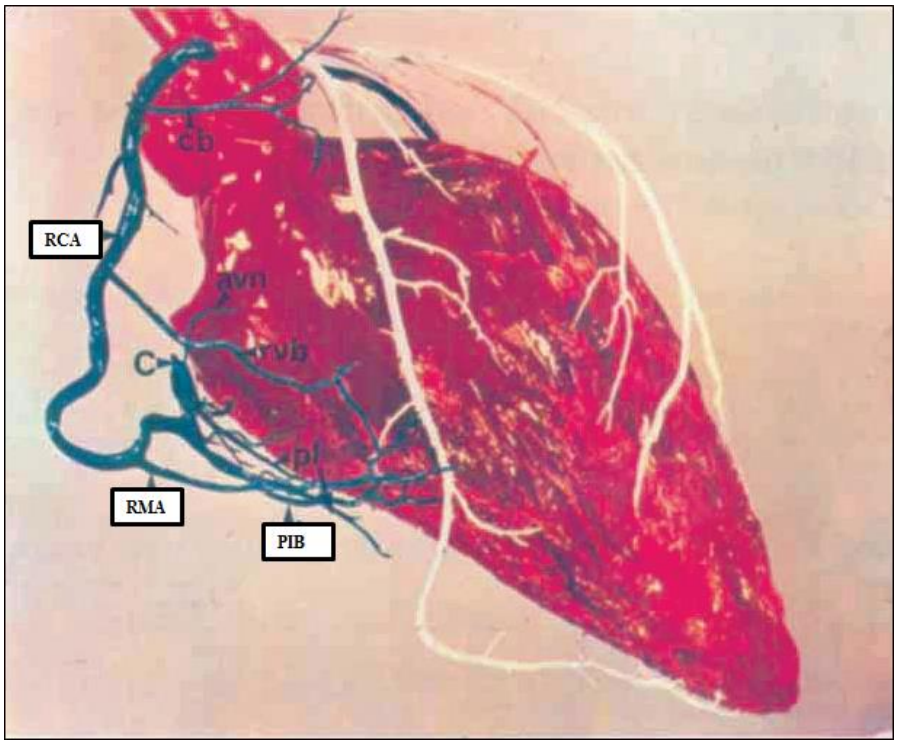

Figure 18*: Cast of the heart showing the RCA and branches in the RAO view (Adapted from Raphael et al., 1980)*

Key: **RCA**- right coronary artery, **RMA**- right marginal artery, **PIB**- posterior interventricular branch, **CB**- conus branch, **RVB**- right ventricular branch, **S**- septal, **AVN**- atrioventricluar node branch

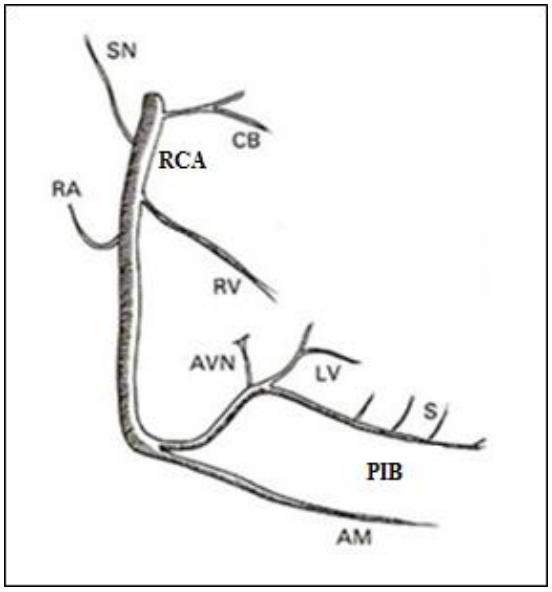

***Figure 19**: Schematic diagram of the RCA and branches in the RAO view (Adapted from Gaze, 2013)*

Key: **RCA**- right coronary artery, **RA**- right atrial branch, **AM**- acute marginal artery (**RMA**- right marginal artery), **PIB**- posterior interventricular branch, **CB**- conus branch, **RV**- right ventricular branch, **S**- septal, **AVN**- atrioventricluar node branch, **LV**- left ventricular branch, **SN**- sinoatrial node branch

2.2.4 CORONARY ARTERIAL SEGMENTS

In order to correctly report coronary arteriographic findings, the standardization of the nomenclature with respect to the assessment and description of the coronary arterial tree is required (Scalon and Faxon, 1999). Standardized systems of coronary arterial classification have been presented by clinical investigators of the Coronary Artery Surgery Study (CASS), Thrombolysis in Myocardial Infarction (TIMI) and Bypass Angioplasty Revascularization Investigation (BARI) trials. The BARI coronary artery map (Figure 20) was derived from the CASS map (Killip *et al*., 1981) with the inclusion

of additional branch segments for the median branch of the LCA, and the possibility of branching of the diagonal, marginal artery and median branch of the LCA (Alderman and Stadius, 1992). The BARI coronary arterial map was also endorsed by the American College of Cardiology/American Heart Association guidelines for coronary angiography (Scalon and Faxon, 1999).

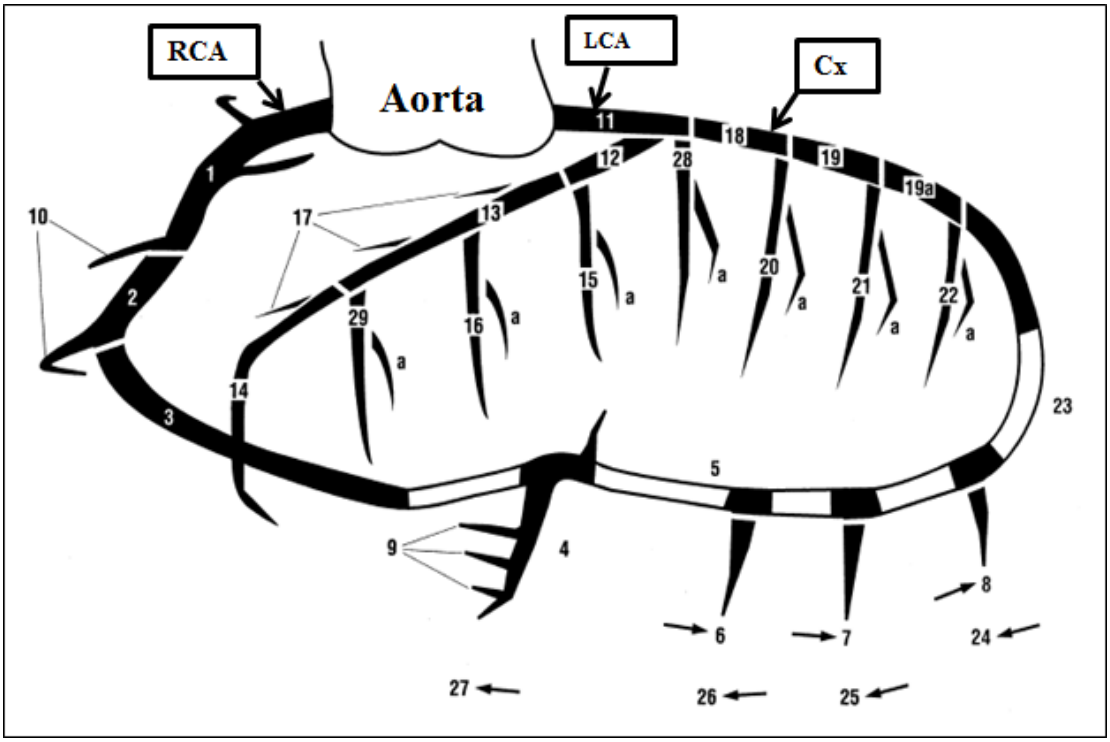

Figure 20: *The Bypass Angioplasty Revascularization Investigation coronary artery map. Right coronary artery:* ***1****-proximal;* ***2****-middle;* ***3****-distal;* ***4****-posterior interventricular branch;* ***5****-right posteroatrioventricular;* ***6****-first posterolateral;* ***7****-second posterolateral;* ***8****-third posterolateral;* ***9****-inferior septal artery;* ***10****- right marginal artery. Left coronary artery:* ***11****-left main;* ***12****-proximal anterior interventricular branch;* ***13****-middle anterior interventricular branch;* ***14****-distal anterior interventricular branch;* ***15****-first diagonal;* ***15a****-first diagonal branch;* ***16****-second diagonal;* ***16a****-second diagonal branch;* ***17****-anterior septals;* ***18****-proximal circumflex;* ***19****-middle circumflex;* ***19a****-distal circumflex;* ***20, 21, 22****- first, second and third left marginal;* ***20a, 21a, 22a****-first, second and third left marginal branches;* ***23****-left atrioventricular;* ***24, 25, 26****-first, second and third posterolaterals;* ***27****-left posterior interventricular branch;* ***28****-Ramus;* ***28a****-Ramus branch;* ***29****-third diagonal;* ***29a****-third diagonal branch*
(Adapted from Alderman and Stadius, 1992).

Key: **LCA**- Left Coronary Artery; **RCA**- Right Coronary Artery; **Cx**- Circumflex branch.

2.3 CORONARY ARTERY ATHEROSCLEROSIS

Atherosclerosis is the main cause of MI and it results from an excessive, inflammatory, fibro-proliferative reaction to various forms of insult or injury to the arterial wall endothelial lining and smooth muscles (Ross, 1981). Although, atherosclerotic lesion development is associated with many systemic risk factors such as hypertension, smoking, diabetes mellitus, and hyperlipidemia, atherosclerosis is mostly a focal disease (Dermibag and Yilmaz, 2005). This is because of the intravascular hemodynamic stress, which is related to the geometry of the vessel (Kirpalani, 1999; Dvir *et al*., 2003) and the anatomic variations in the arterial wall are important focal factors in atherosclerosis (Ross, 1981).

2.3.1 DISTRIBUTION OF ATHEROSCLEROTIC LESIONS IN THE CORONARY ARTERIES

Atherosclerotic lesions are not usually randomly distributed and are preferentially situated at branch ostia, bifurcation points, and the proximal segments of the resulting daughter vessels (Asakura and Karino, 1990; Park and Park**,** 2009). The morphology of the LCA has also been reported to influence the distribution of atherosclerotic lesions in its branches (Ajayi *et al*., 2013b). The presence of atherosclerotic lesions in main coronary arteries such as the RCA, anterior interventricular branch or circumflex branch is regarded as *single*, *double* and *triple vessel coronary artery disease* when *one*, *two* or *all three* of these vessels are affected, respectively.

2.4 CORONARY COLLATERAL PATHWAYS

2.4.1 HISTORICAL PERSPECTIVE

In the 17th century, as the study of the circulatory system progressed, Lower (1631-1691) was the first to demonstrate the presence of anastomosis between different branches of the same or different coronary arteries (van Royen *et al*., 2001; Vilallonga, 2003). Albrecht von Haller, a Swiss anatomist in the 18th century, corroborated Lower's observation. In the following century, investigators using human cadaveric dissections declared that the coronary arteries were end arteries, and hence, do not anastomose with one another (Loukas *et al*., 2009a). Therefore, traditionally, the myocardium had no regions of overlapping coronary arterial supply (Traupe *et al*., 2010).

This belief continued until the 20th century when Spalteholtz (1924) demonstrated the presence of coronary anastomoses in a post-mortem angiographic study (Loukas *et al*., 2009a). Subsequently, studies using cadaveric hearts corroborated these findings. Baroldi *et al*. (1956) demonstrated the presence of coronary collaterals in normal human hearts at autopsy and showed that the number of coronary collaterals was increased in hearts with the presence of coronary artery disease (Koerselman *et al*., 2003; Schaper, 2009). Their study provided the best evidence that the human coronary arteries are not end-arteries; however, an arteriolar network interconnects them (Schaper, 2009). In a post-mortem examination, Fulton (1964) later supported this finding and reported that a higher number of large-caliber coronary collaterals were associated with a longer history of angina (Koerselman *et al*., 2003).

2.4.2 DEVELOPMENT OF THE CORONARY COLLATERAL PATHWAYS

Coronary collateral arteries have their origin from the same embryonic precursor as the native coronary arteries during embryogenesis; therefore the foundation of these collateral arterial network is laid down during embryonic life (Loukas *et al*., 2009a) and are present in the newborn (Schaper, 2009). The normal human heart contains interconnecting channels (Levin, 1974), hence, coronary collateral pathways are present in both normal and diseased hearts (Meier *et al*., 2012). These channels exist as microvessels whose function are not clear (Rockstroh and Brown, 2002) and are not demonstrable angiographically when coronary circulation is normal or mildly obstructed (Levin, 1974).

Functional collaterals were suggested to have developed from hypertrophic evolution of the vessels present in the normal heart (Koerselman *et al*., 2003). This evolutionary process is triggered by myocardial ischaemia and/or an increase in the pressure gradient in the collateral network (Sasayama and Fujita, 1992; Schaper, 2009; Chilian *et al*., 2012). Due to this pressure gradient, there is an increase in the volume of blood propelled through these channels. They progressively dilate and are eventually angiographically visible as coronary collateral channels (Levin, 1974). The pressure gradient also results in an increased fluid shear stress in the vessel (Landwiniec and Hoye, 2013). This fluid shear stress is a primary morphogenic physical factor that determines the size of the developing collateral vessel (Schaper, 2009).

The most potent stimulus and important predictor for the development of coronary collaterals is coronary arterial stenosis (Seiler, 2003; Meier *et al*., 2012) and the resultant change in pressure gradient between the high pre-occlusive and the low post-occlusive pressure regions interconnected by coronary collaterals (Schaper, 2009). However, there are other factors that also contribute to this process, and these include the size and condition of the distal segmental lumen of the vessel, blood viscosity, myocardial contractility, coronary vascular resistance (Levin, 1974), and physical activity of the subject (Senti *et al*., 1998). Medical condition such as diabetes mellitus has been reported to adversely affect the development of functional coronary collateral circulation (Abaci *et al*., 1999; Tatli *et al*., 2007). Contrary to the latter finding, Zbinden *et al*. (2005) found that there was no difference in the coronary collateral flow between diabetic and non-diabetic patients.

2.4.3 MECHANISM OF CORONARY COLLATERAL GROWTH

ARTERIOGENESIS VERSUS ANGIOGENESIS

Vasculogenesis refers to the earliest events in vascular growth during which endothelial cell precursors (angioblasts) move to distinct locations, differentiate and assemble into solid endothelial cords. These cords later form a vascular plexus with the endothelial tubes (Figures 22 and 23) (Conway *et al*., 2001). Therefore, the term vasculogenesis is strictly reserved for the development of new blood vessels during embryogenesis (Buschmann and Schapper, 2000).

Angiogenesis is the process by which these primitive vascular cords are transformed into mature vascular networks through their growth, expansion and remodelling (Conway *et al.*, 2001). In this process, pre-existing capillaries multiply and develop new capillary networks and these newly formed capillary tubes are devoid of vascular smooth muscles (Figures 22 and 23) (Buschmann and Schapper, 2000).

Arteriogenesis is the process of development of new capillaries by growth and intussusception of pre-existing capillaries after an arterial occlusion with the maturation of arteries from pre-existing interconnecting arterioles (Cai and Schaper, 2008) (Figures 21 and 22). Although it has some similar features with angiogenesis, its pathway is different. An occluded artery can potentially be totally replaced through arteriogenesis, whereas, angiogenesis cannot achieve this (Cai and Schaper, 2008). The development and maturation of collateral vessels results in channels that are capable of carrying a significant amount of blood (Annex and Simons, 2005), therefore, coronary collateral vessels develop through arteriogenesis (Meier *et al*., 2013).

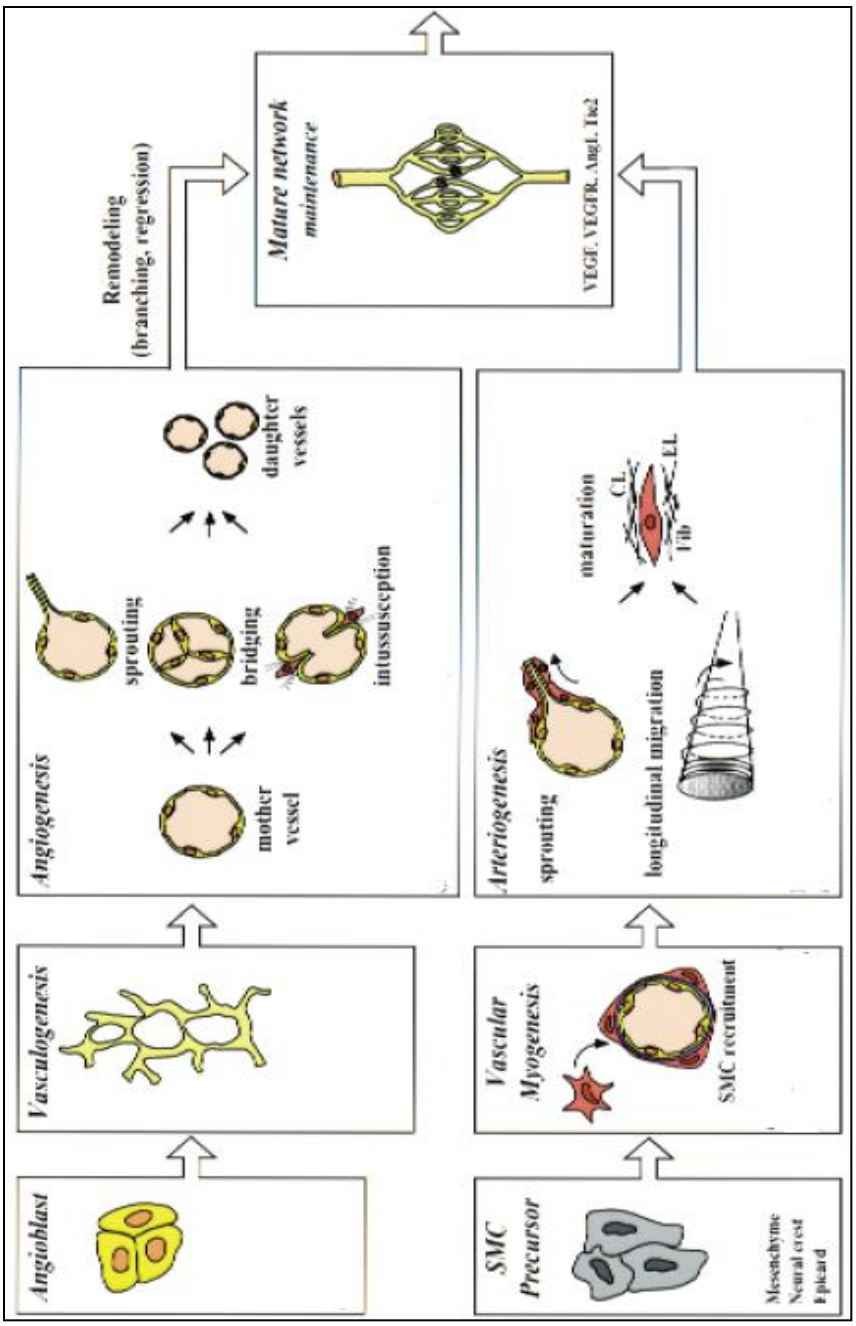

Figure 21*: Schematic diagrams showing the processes of vascular growth in an embryo, endothelial precursors (angioblasts) assemble in a primitive network (vasculogenesis), that expands and remodels (angiogenesis). Smooth muscle cells cover endothelial cells during vascular myogenesis, and stabilize vessels during arteriogenesis.*
(Adapted from Carmaliet, 2000)

Key: **SMC**- smooth muscle cell, **CL**- collagen, **EL**- elastin, **Fib**- fibrillin, **VEGF** – Vascular endothelial growth factor, **VEGFR**- Vascular endothelial growth factor receptor, **Ang** - Angiopoietin

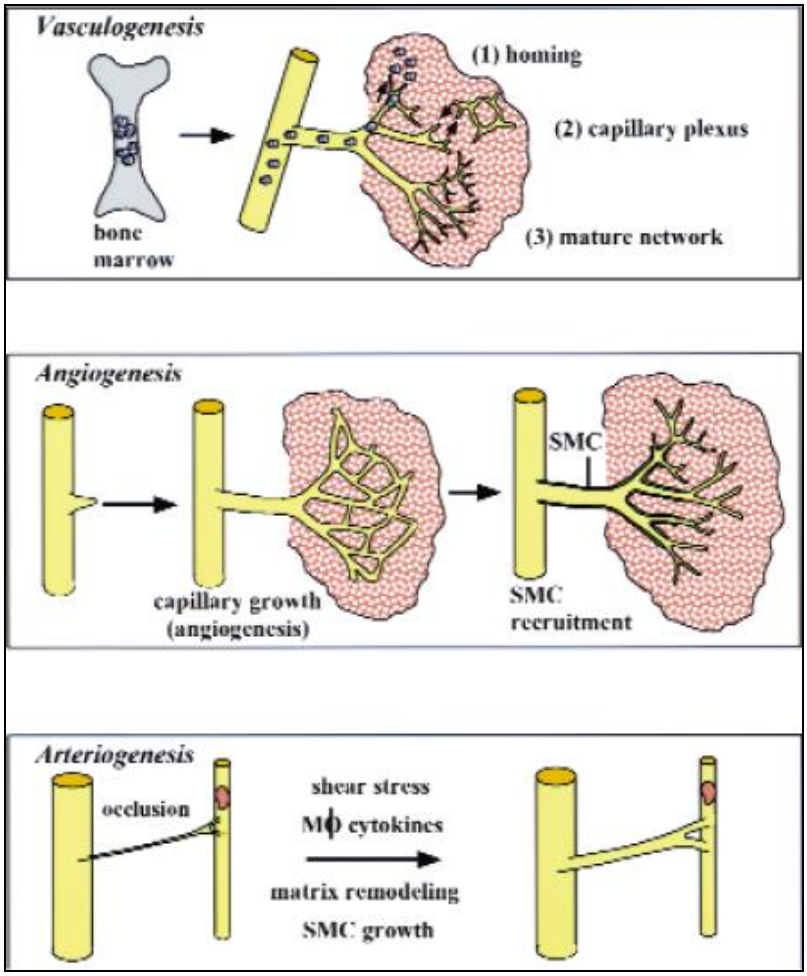

Figure 22*: Schematic diagrams showing the processes of pathological vascular growth in an adult, vasculogenesis (angioblast mobilization), angiogenesis (sprouting) or arteriogenesis (collateral growth). (Adapted from Carmaliet, 2000)*

Key: **SMC**- smooth muscle cell, **MØ**- macrophage

2.4.4 MORPHOLOGY OF THE CORONARY COLLATERAL PATHWAYS

Coronary collateral arterial pathways are abundant in the heart and serves as an "innate coronary arterial bypass" within the main coronary arteries (Loukas *et al*., 2009a). These channels are of variable sizes and allow for bi-directional flow between the main coronary arteries (Miyamoto *et al*., 2000). The coronary collaterals have a number of definable pathways unlike collaterals in other regions of the body such as the thigh and the knee; therefore, these vessels do not wander randomly through the myocardium (Levin *et al*., 1973). From the literature reviewed, the most extensive description of the pathways of the coronary collaterals to date was reported by Levin in 1974. In this study conducted in North America, a list of 22 collateral pathways was compiled. Some of these identified collateral arterial pathways were similar, being mentioned twice because they were visualized in patients with different coronary arterial occlusions.

There is great variability in the pattern and the extent of these coronary collateral pathways among different population groups (Loukas *et al*., 2009a). Variability also exists in an individual's ability to develop coronary collateral arteries, some individuals develop functional collateral vessels, while others do not (Turgut *et al*., 2009; Ladwiniec and Hoye, 2013; Meier *et al*., 2013). From the literature reviewed, it is apparent there is no study documenting the systematic identification of the anatomic pathways and grading of coronary collateral vessels. Some researchers have assessed the effect of age and sex on the development of functional coronary collateral vessels. However, the relationship between the morphological properties of the coronary arteries and the development of functional coronary collateral vessels has not been evaluated.

Wustman *et al*. (2003) reported the presence of adequately functional collaterals in 20-25% of patients with angiographically normal coronary arteries, while Pohl *et al*. (2001) found these collaterals in 33% of patients with coronary artery disease. The reason for this is not understood (Meier *et al*., 2013), and presently, there is no explanation for the differences between the capabilities of individuals to develop a sufficient collateral circulation (Koerselman *et al*., 2003). However, genetic factors may affect the development of functional collaterals (Chittenden *et al*., 2006) with the possibility of up/down regulation of the genes involved in the formation of these collateral vessels prior to the occurrence of coronary artery disease (Seiler, 2003) . Nevertheless, the potential of an individual to develop coronary collateral circulation is thus far not adequately examined (Koerselman *et al*., 2003).

2.4.5 ASSESSMENT OF THE CORONARY COLLATERAL PATHWAYS

I. Coronary angiography

Cineangiographic coronary arterial images have been the major method for the determination of coronary arterial luminal stenosis (Scanlon and Faxon, 1999). The easiest and most commonly used method of coronary collateral assessment is by coronary angiography (Werner *et al*., 2003; Meier *et al*., 2013). Coronary collateral circulation can be visualized during coronary angiography (Koerselman *et al*., 2003), therefore, it is a helpful diagnostic technique for demonstrating the coronary collaterals (Husanović *et al*., 2005). Most studies have assessed coronary collaterals using coronary angiography and this method has been used in determining the presence and grading of the coronary

collateral pathways (Figure 23). In the absence of total occlusion of the vessel, the assessment of recruitable coronary collaterals can be performed by the insertion of two coronary catheters; one is for balloon occlusion of the collateral receiving stenosed vessel, while the second is for the injection of contrast dye into the normal collateral supplying vessel (Seiler, 2003).

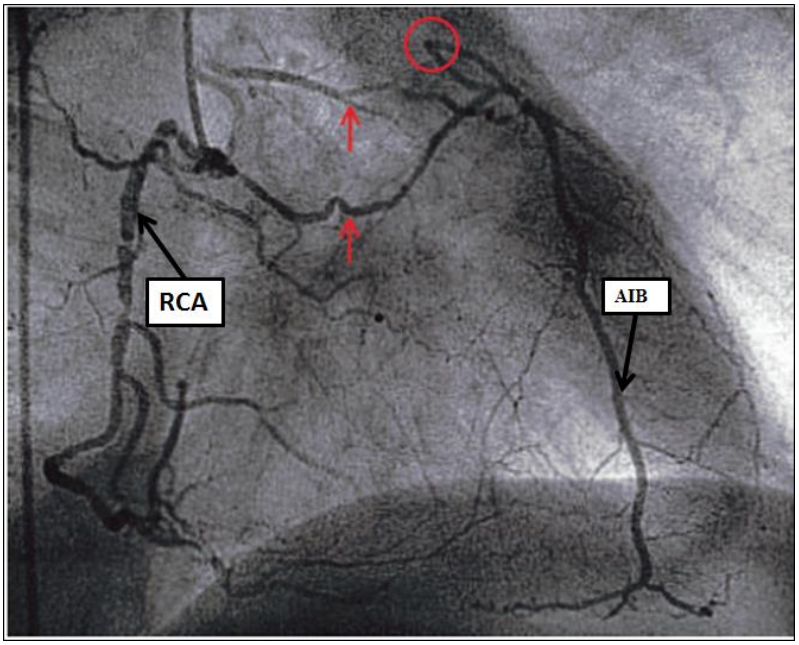

Figure 23*: Coronary angiogram with injection of radiographic contrast medium into the RCA and complete filling of the proximally occluded (red circle) anterior interventricular branch via collateral channels (red arrows) (Adapted from Seiler et al., 2003)*

Key: **AIB**= anterior interventricular branch, **RCA**= right coronary artery

II. Collateral flow index (CFI)

There are two methods available for the assessment of coronary collaterals using the CFI: one depends on intra-coronary Doppler velocity measurement, while the other depends on intra-coronary pressure measurement (Meier *et al*., 2013). The CFI is an expression of the flow through the collaterals as a fraction of the flow in the normally patent vessel

(Seiler *et al*., 1998). Poor collateralization of the obstructed vessel was defined by a CFI of < 0.25 (Meier *et al*., 2012).

a) Velocity-based CFI (CFI_v)

The measurement of collateralization of a stenosed coronary artery was done by the placement of a Doppler sensor tipped guide wire distal to the stenosis. The anterograde flow through the stenosed coronary artery was blocked with an angioplasty balloon (Figure 25). Therefore, the flow velocity measured with the Doppler sensor distal to the occluded vessel is from coronary collaterals. Afterwards, angioplasty of the stenosed vessel was performed, thereby removing the lesion. The flow velocity was subsequently re-measured, which represented the flow through the normal vessel. The collateral flow velocity measured was then compared to the flow velocity recorded through the open coronary artery. This indicated a fraction of normal blood flow that can be supplied through the collateral circulation in case of a sudden occlusion of the vessel (Meier *et al*., 2013).

b) Pressure-based CFI (CFI_p)

The CFI_p is measured with the aid of a pressure sensor tipped coronary guide wire, which is placed distal to the stenotic lesion in the diseased vessel (Figure 24). The collateral flow index was calculated from the pressure measured after the occlusion of the vessel (P_{occl}) by inflation of the catheter balloon and the pressure proximal to the balloon occlusion (mean aortic pressure [P_{ao}]). The central venous pressure (CVP) was subtracted from these two pressures to correct for the back pressure: $CFI = (P_{occl} - CVP) \div (P_{ao} - CVP)$ (Meier *et al*., 2012). The CFI_p theoretically corresponds to the CFI_v (Seiler *et al*., 1998).

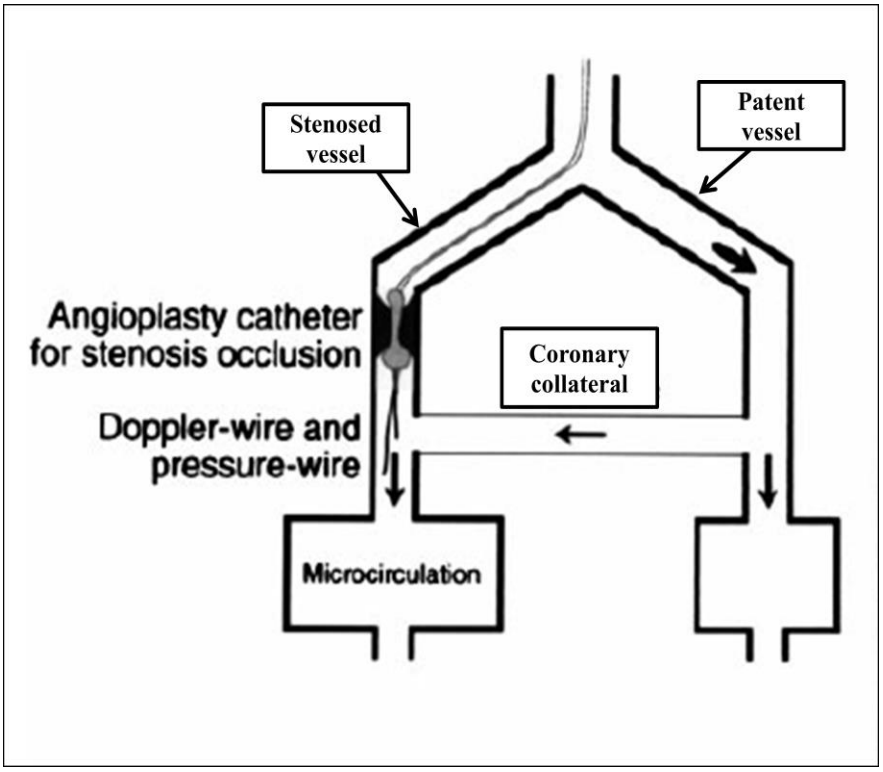

Figure 24*: Schematic diagram of the coronary collateral circulation with an inflated angioplasty balloon and a Doppler and pressure guidewire located distal to the stenosis. (Adapted from Seiler et al., 1998)*

III. Positron emission tomography

Demer *et al*. (1990) demonstrated the use of positron emission tomography as a non-invasive method of quantify coronary collateral circulation to the myocardial region subtended by a vessel with coronary artery disease. The study evaluated the effect coronary collaterals on myocardial perfusion in patients with well-developed collaterals as compared to those without collateralization. The study concluded that non-invasive evaluation of myocardial perfusion may be beneficial in investigating the clinical importance of coronary collaterals and thereby improving clinical decision making.

IV. Echocardiography

The introduction of new generation echo contrast agents and advanced ultrasound techniques such as myocardial contrast echocardiography (MCE) has led to an indirect assessment of collateral derived myocardial perfusion (Baroldi *et al*., 2005). MCE is an ultrasound imaging technique that utilizes physiologically inert gas-filled microbubbles. The microbubbles being biologically inert are safe and remain entirely within the vascular space. They have an intravascular rheology that is very similar to that of the red blood cells and respond nonlinearly to ultrasound (Kaul, 2008). MCE was used to track the course of collateral growth, and was suggested as a powerful tool for non-invasively mapping coronary collateral development through therapeutic angiogenesis (Mills *et al*., 2000). Vogel *et al*. (2006) with the use of MCE during angioplasty validated the use of pressure-derived CFI to determine collateral-derived myocardial blood flow.

2.4.6 CLASSIFICATION OF THE CORONARY COLLATERAL PATHWAYS

2.4.6.1 ANATOMIC CLASSIFICATION

Several authors have used different methods in describing and defining the coronary collateral pathways. May (1960) classified the coronary collateral vessels based on the relationship of these vessels with other coronary vessels and the area of MI. These vessels were classified anatomically into four categories as follows:-

a) **Bypass collaterals**: They are channels that extended around a segment of atheromatous occlusion of a vessel. These channels connect the proximal portion of the obstructed vessel to its distal portion and are most visible where the obstruction is of short length (Figure 25).

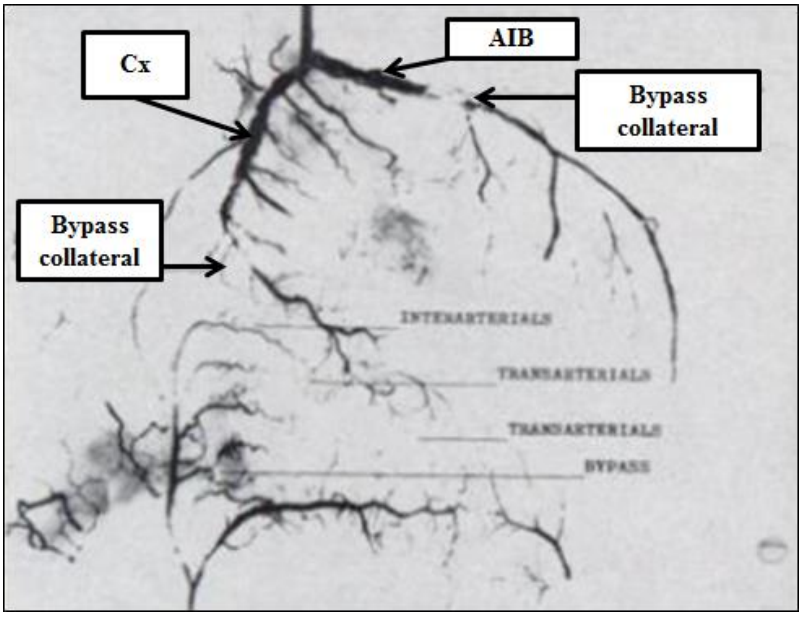

Figure 25: *Bypass collaterals in the total occlusion of the anterior interventricular and the circumflex branches (Adapted from May, 1960)*

Key: **AIB**= anterior interventricular branch, **Cx**= circumflex branch

b) **Interarterial collaterals**: These are anastomotic channels that joined the secondary branches of the same coronary artery (Figure 26).

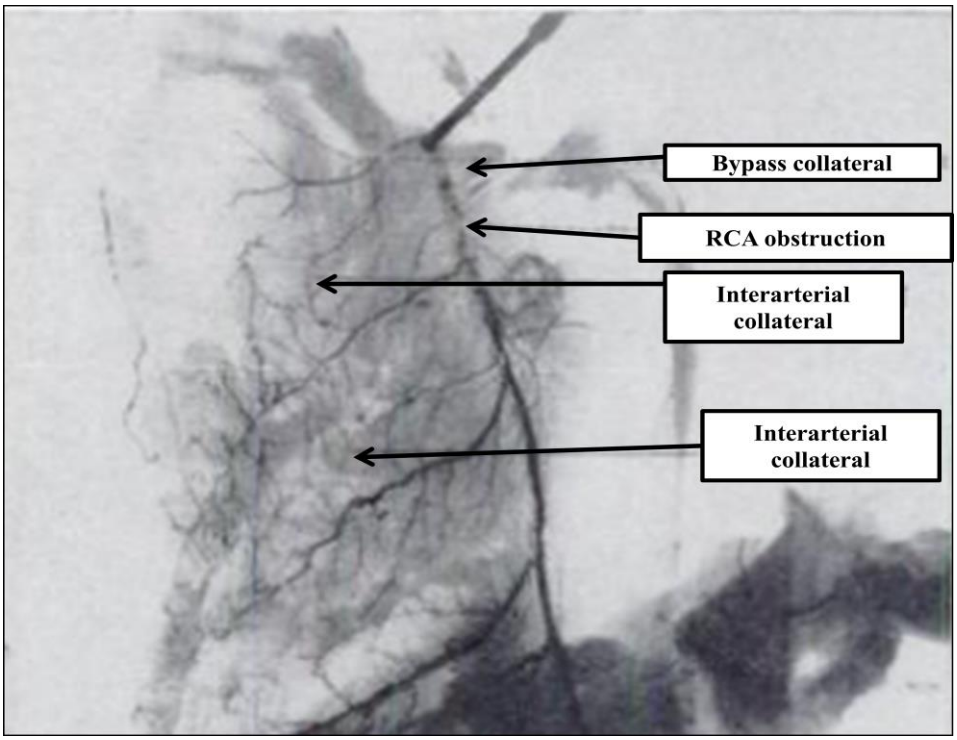

Figure 26: *Interarterial collaterals between RCA branches in the occlusion of the RCA (Adapted from May, 1960)*

Key: **RCA**= right coronary artery

c) **Transarterial collaterals**: They are those channels that connect the RCA and LCA in the septal region at either the anterior or posterior interventricular regions (Figure 27).

d) **Scar collaterals**: They originated from adjacent vessels near an area of infarction, are numerous and course into and through the scar area. They are regarded as newly formed vessels and not the enlargement of previously formed vessels.

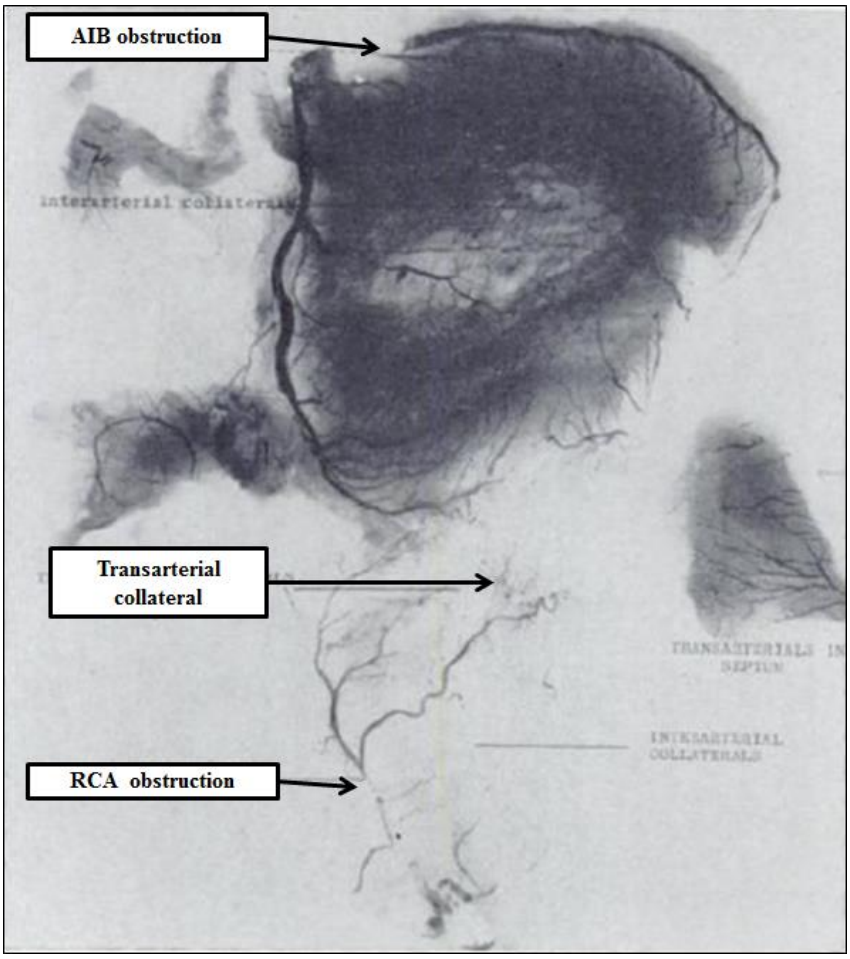

Figure 27: *Transarterial collaterals between RCA and LCA branches in the occlusion of the RCA (Adapted from May, 1960)*

Key: **AIB**= anterior interventricular branch, **RCA**= right coronary artery

Some years after the description of the coronary collaterals by May (1960), Paulin (1967) in a coronary angiographic study of patients with advanced coronary arterial obstruction described more pathways of the coronary collaterals. In his study, 10 different pathways of the coronary collateral arteries were documented.

i) **Septal collaterals**: These are anastomotic vessels in the interventricular septum creating arterial connections between anterior interventricular branch and the posterior interventricular branch (Figure 28i).

ii) **Epicardial collaterals of right ventricular wall**: They are connections between the largest branch of the RCA near the right ventricular wall and the anterior interventricular branch (Figure 28ii).

iii) **Collaterals in the moderator band**: These are channels which run in the moderator band connecting the largest septal branch of the anterior interventricular branch to the largest branch of the RCA at the right ventricular wall (Figure 28iii).

iv) **Collaterals in the crista supraventricularis**: They are anastomotic channels arising from the second or third branch of the RCA and are connected to already present septal collaterals or AV node artery. These vessel move either through the superior or inferior region of the interventricular septum (Figure 28iv).

v) **Epicardial collaterals of pulmonary conus**: These are anastomoses similar to the arterial ring of Vieussens, located around the root of the pulmonary

trunk. They are communications between the conal branches of the RCA and the anterior interventricular branch (Figure 28v).

vi) **Direct-bypass collaterals at site of occlusion**: These are channels connecting the proximal part of an obstructed artery with the distal part of the same artery (Figure 28vi).

vii) **Epicardial collaterals at apex**: Anastomoses between the distal extension of the anterior interventricular branch and the posterior interventricular branch at the apical region (Figure 28vii).

viii) **Collaterals of the left ventricular wall**: Small vessels connecting the distal extension of the circumflex branch with either branches of the anterior interventricular branch or the RCA (Figures 28viii and ix).

ix) **Collaterals in the atrial walls**: Collateral connection between the proximal RCA and circumflex branch dorsal to the aorta at the level of the atrial walls. They include SA node arteries of either side from which a small-calibre vessel branch off and moved toward the contralateral side of the heart (Figure 28x).

x) **Collaterals from bronchial arteries**: Branches from bronchial areteries extending to the region of the atria, however, unequivocal connection between these vessels and the coronary arteries was not established.

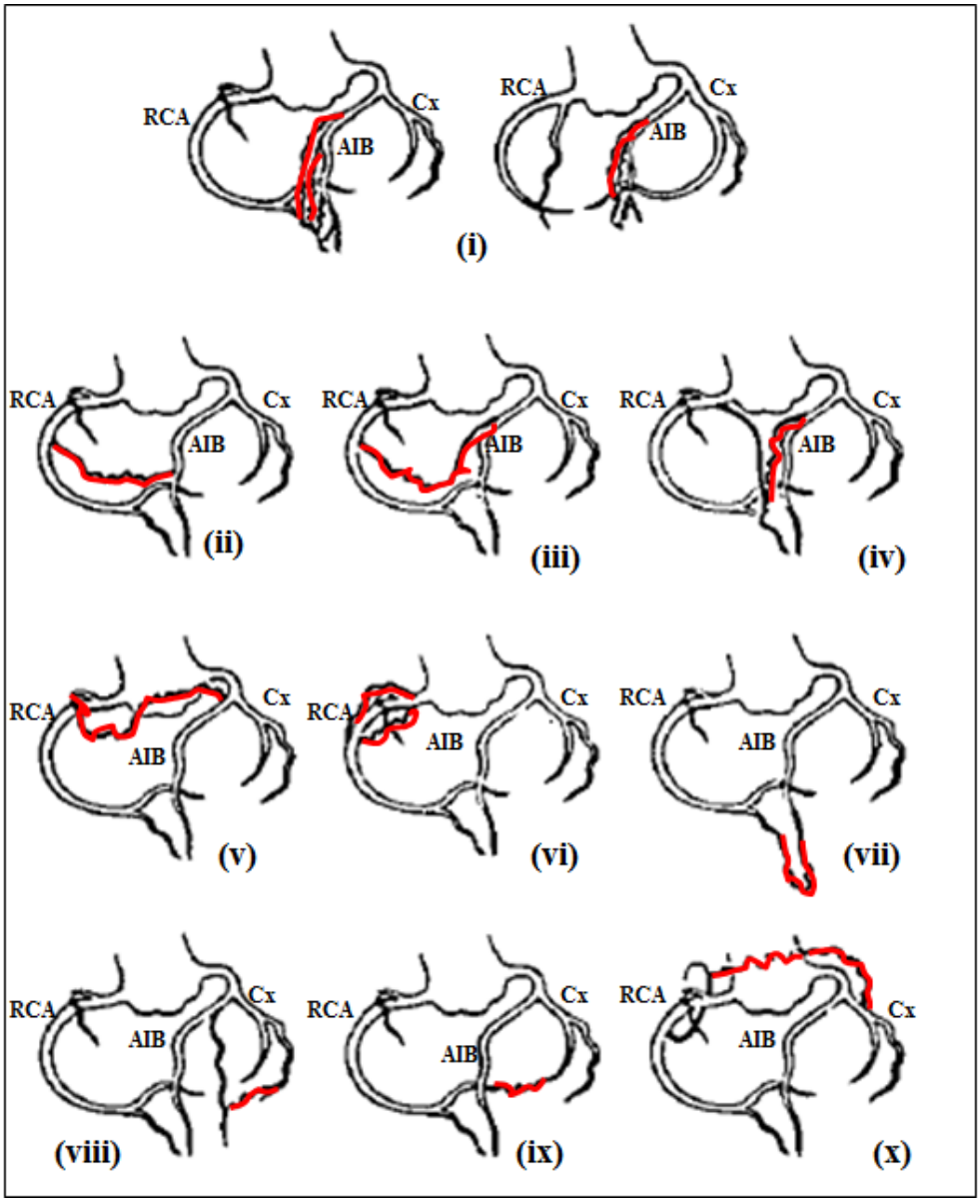

Figure 28 (i-x): *The different collateral connections (highlighted in red) in the presence of significant coronary arterial obstruction (Adapted from Paulin, 1967)*

Key: **AIB**= anterior interventricular branch, **RCA**= right coronary artery, **Cx**= circumflex branch

The most extensive description of the coronary collateral pathways to date was done by Levin in 1974. In this study, coronary angiograms obtained from patients with significant coronary artery disease and total coronary arterial obstructions were used. A total of 22 coronary collateral pathways were described. In the obstruction of the RCA, ten pathways were documented as follows:-

i) Collateral channels from the anterior interventricular branch to the posterior interventricular branch of the RCA via septal branches (Figure 29i).

ii) Collaterals between distal circumflex branch and the distal RCA (Figure 29ii)

iii) Arteries joining the left marginal branch of the circumflex branch to posterior left ventricular branch of RCA (Figure 29iii).

iv) Collateral arteries connecting the proximal right marginal branch or CB to distal right marginal branch of the RCA (Figure 29iv).

v) Kugel's artery, which connects either the proximal part of the RCA or LCA to the AV node branch of the distal RCA by running along the anterior margin of the atrial septum (Figure 29v).

vi) Collateral arteries joining the distal anterior interventricular branch extending around the cardiac apex to posterior interventricular branch of the RCA (Figure 29vi).

vii) An anastomosis from the distal segment of the circumflex branch or its left atrial circumflex branch to AV node branch of the RCA (Figure 29vii).

viii) Vessels from the right marginal branch of the RCA to posterior interventricular branch of the RCA through the diaphragmatic surface of the right ventricle (Figure 29viii).

ix) Anastomotic channels from the SA node branch of the RCA which runs around the lateral wall of the left atrium to left atrial circumflex branch and then to the distal segment of the RCA (Figure 29ix).

x) Coronary collateral channels between the right ventricular branch of the anterior interventricular branch and the right marginal branch of the RCA (Figure 29x).

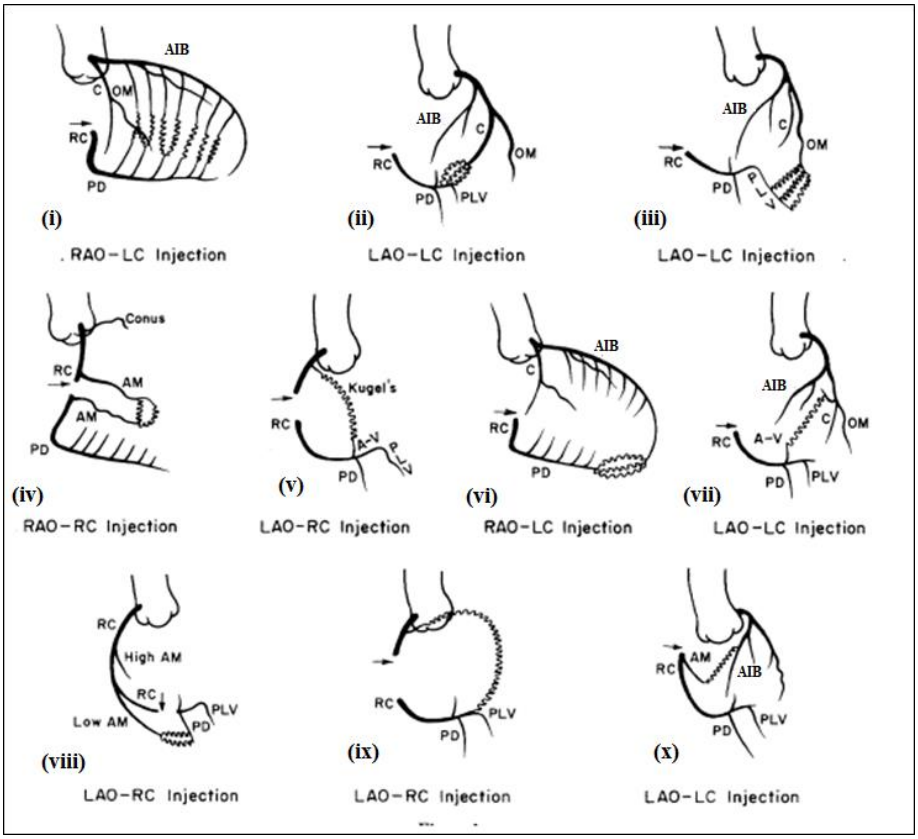

Figure 29(i-x): *Collateral pathways in RCA obstruction (Adapted from Levin, 1974)*

Key: **LAO**= left anterior oblique projection, **RAO**= right anterior oblique projection, **LC** = left coronary artery, **RC** = right coronary artery, **AIB**= anterior interventricular branch, **C**= left circumflex branch (**Cx**= circumflex branch), **AM**= acute marginal (**RMA**= right marginal artery); **PD**= posterior descending branch of the right coronary artery (**PIB**= posterior interventricular branch), **PLV**= posterior left ventricular branch right coronary artery, **A-V** atrioventricular node artery, **LM**= left marginal branch circumflex branch

In the patients with total occlusion of the anterior interventricular branch in this study by Levin (1974), seven collateral pathways were recorded as follows:

i) Arteries joining the AM branch of the RCA to the anterior interventricular branch (Figure 30i).

ii) Anastomotic channels between the proximal septal branch of the anterior interventricular branch and a more distal septal branch of the anterior interventricular branch (Figure 30ii).

iii) Collateral vessels between the left marginal branch of the circumflex branch and the anterior interventricular branch (Figure 30iii).

iv) Vessels joining the CB of the RCA to the anterior interventricular branch (Figure 30iv).

v) Anastomosis between the diagonal branch of the anterior interventricular branch and the distal segment of the anterior interventricular branch (Figure 30v).

vi) Collateral channels moving around the cardiac apex that joins the posterior interventricular branch of the RCA to the anterior interventricular branch (Figure 30vi).

vii) Anastomoses between the posterior interventricular branch of the RCA and the anterior interventricular branch via septal branches (Figure 30vii).

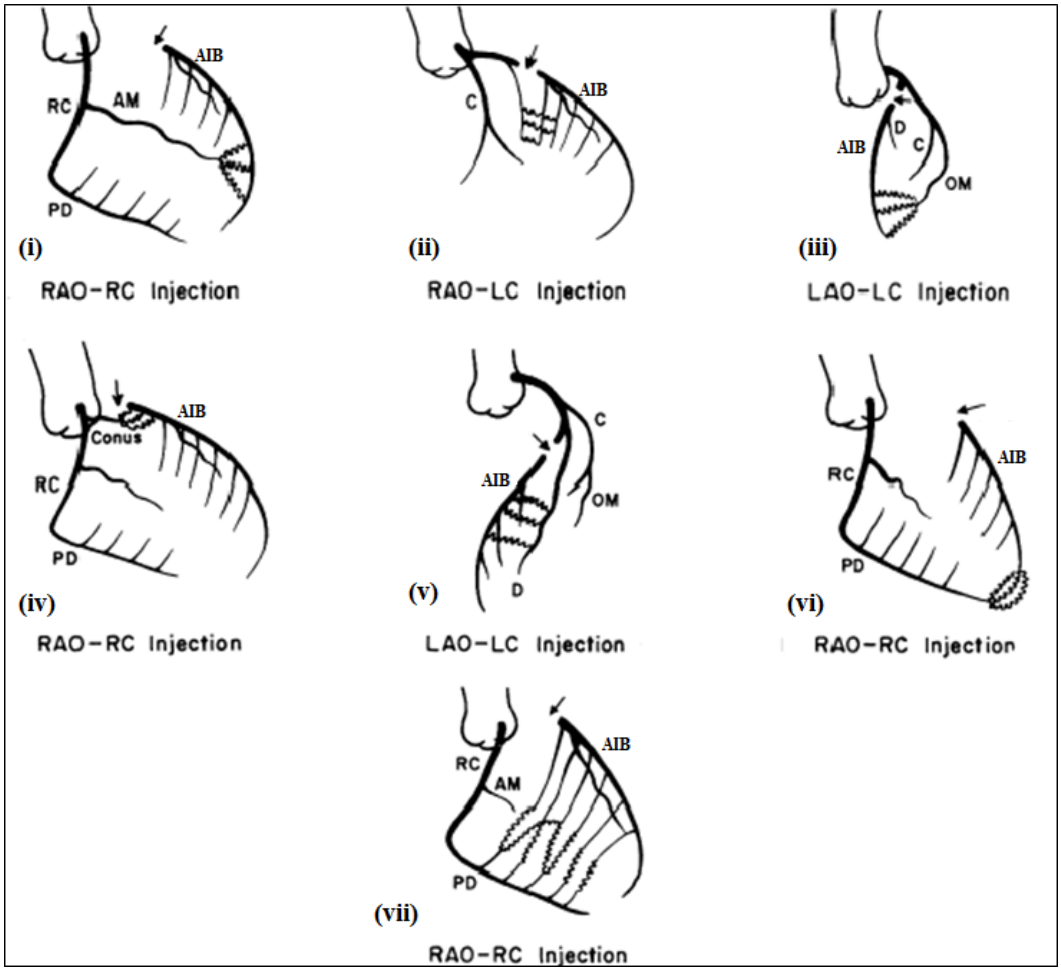

Figure 30(i-vii): *Collateral pathways in anterior interventricular branch obstruction (Adapted from Levin, 1974)*

Key: **LAO**= left anterior oblique projection, **RAO**= right anterior oblique projection, **LC** = left coronary artery, **RC** = right coronary artery, **AIB**= anterior interventricular branch, **C**= left circumflex branch, **AM**= acute marginal (**RMA**= right marginal artery); **PD**= posterior descending branch of the right coronary artery (**PIB**= posterior interventricular branch), **PLV**= posterior left ventricular branch right coronary artery, **A-V** atrioventricular node artery, **LM**= left marginal branch circumflex branch, **D**= diagonal branch of the left anterior descending (diagonal branch of the anterior interventricular branch).

The least number of stenotic lesions were observed in the circumflex branch, five collateral pathways were documented in cases of the obstruction of this artery. These collateral pathways are listed below.

i) The union of left atrial circumflex branch to the distal segment of the circumflex branch (Figure 31i).

ii) Connection of the proximal left marginal branch of the circumflex branch to a more distal left marginal branch by collaterals (Figure 31ii).

iii) Collateral vessels joining the diagonal branch of the anterior interventricular branch to the left marginal branch of the circumflex branch (Figure 31iii).

iv) Channels connecting the distal RCA to the distal circumflex branch (Figure 31iv).

v) Collaterals between the posterior left ventricular branch of the RCA and the left marginal branch of the circumflex branch (Figure 31v).

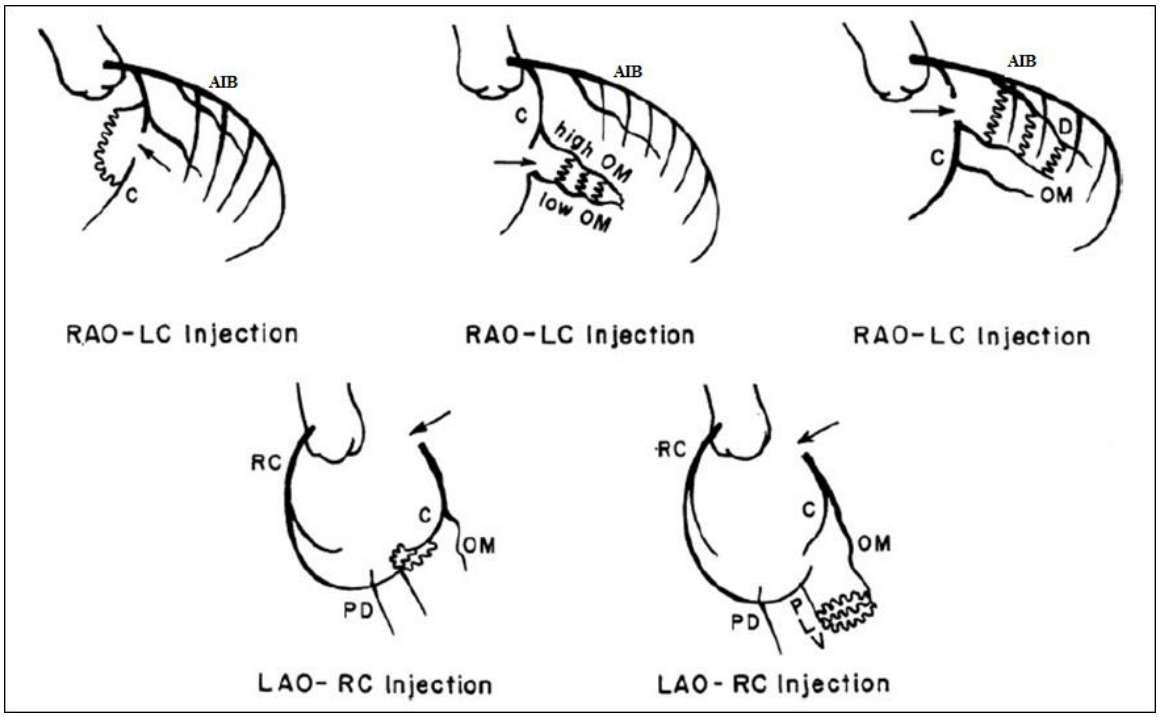

Figure 31(i-v): *Collateral pathways in circumflex obstruction (Adapted from Levin, 1974)*

Key: **LAO**= left anterior oblique projection, **RAO**= right anterior oblique projection, **LC** = left coronary artery, **RC** = right coronary artery, **AIB**= anterior interventricular branch, **C**= left circumflex branch, **AM**= acute marginal (**RMA**= right marginal artery); **PD**= posterior descending branch of the right coronary artery (**PIB**= posterior interventricular branch), **PLV**= posterior left ventricular branch right coronary artery, **A-V** atrioventricular node artery, **LM**= left marginal branch circumflex branch, **D**= diagonal branch of the left anterior descending (diagonal branch of the anterior interventricular branch).

Rockstroh and Brown (2002) used a different system of classification in which the collateral arteries divided into *four* anatomical types. The arteries were named according to the flow from the donor to the recipient artery, and the diameter of the vessels was graded on a numerical scale from one to three. The coronary collaterals were classified as follows: - *septal, atrial, ventricular free wall branc*h and *bridging* vessels (Figure 32).

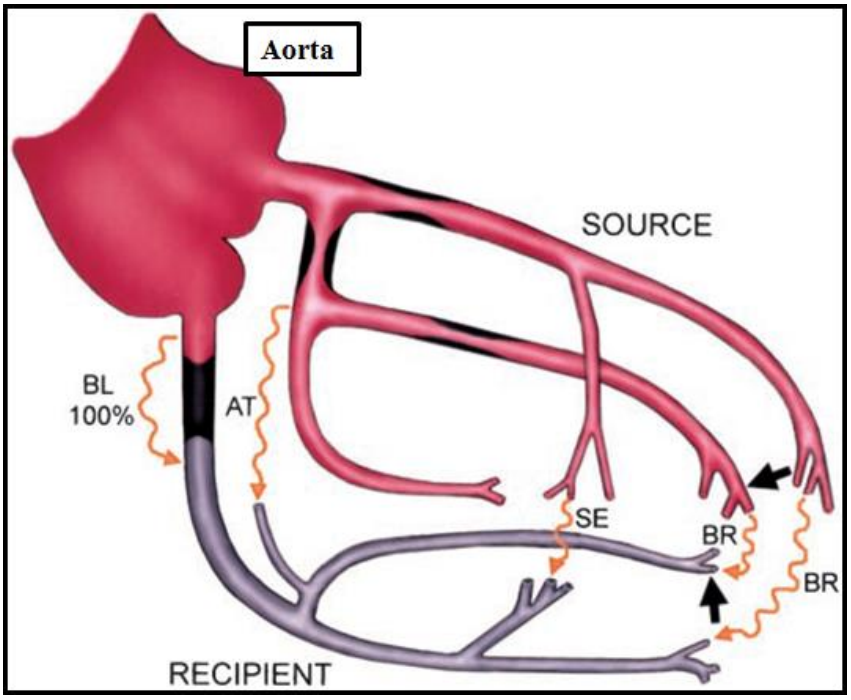

Figure 32: *Schematic diagram showing the classification of coronary collaterals by Rockstroh and Brown (2002) (Adapted from Rockstroh and Brown, 2002)*

Key: **AT**= atrial, **BL**= bridging, **BR** = ventricular free wall, **SE** = septal

2.4.6.2 FUNCTIONAL GRADING OF CORONARY COLLATERAL VESSELS

Functionally, different grading systems have been developed for the coronary collaterals. These grading systems were used to evaluate the significance of the collateral vessels in preserving vascular supply to the myocardial region subtended by a stenosed or an obstructed coronary artery.

(a) Using the swiftness and intensity of opacification

Wainwright *et al*. (1980) angiographically graded coronary collateral vessels based on the swiftness and intensity of opacification of the vessels with the contrast medium. The collateral vessels were graded as follows:-

Grade 0: absence of coronary collateral vessels

Grade 1: poorly developed coronary collateral vessels with no prominent distal channel visualized during angiography

Grade 2: moderate coronary collaterals giving faint but delayed opacification of a prominent distal channel

Grade 3: good coronary collaterals giving clear opacification of a prominent distal channel

Grade 4: excellent coronary collaterals giving full and brisk opacification of prominent distal vessels.

(b) Using collateral filling of the obstructed vessel

The most commonly used grading system by researchers is the Rentrop classification (Seiler *et al*., 2001) which is based on the collateral filling of the epicardial artery. This grading system was proposed by Rentrop *et al*. (1985). However, Werner *et al*. (2003)

reported a weak correlation between this grading system and invasive parameters of collateral function. Collateral filling of the obstructed vessel was graded as follows:-

Grade 0: no filling

Grade 1: filling of side branches only without visualization of the epicardial segment

Grade 2: partial filling of the epicardial segment of the obstructed vessel

Grade 3: complete filling of the epicardial segment of the obstructed vessel.

(c) Using quality of flow into the segment of the vessel distal to the lesion

The Bypass Angioplasty Revascularization Investigation (BARI) group defined coronary collateral function in terms of the quality of flow into the vessel distal to an obstructing lesion (Alderman and Stadius, 1992). The collaterals were graded as follows:

No visible flow: where the contrast did not flow distal to the region of obstruction

Poor: the presence of small amount of flow and incomplete opacification of the distal vessel.

Good: there was slowed distal filling, but the distal vessel was completely opacified.

Excellent: there was prompt flow into the vessel with rapid clearing of the contrast.

(d) Washout collaterometry

Seiler *et al*. (2001) described an angiographic method of assessing the function of coronary collaterals using washout of contrast dye. In this method, a contrast dye was injected into the stenosed vessel prior to the occlusion of the vessel with a balloon. The number of heart beats needed to wash out the contrast dye injected into the coronary artery immediately after occlusion was determined. The contrast dye caught distal to the occlusive balloon was washed out by collateral flow and a cut of value of 11 heart beats

for contrast washout was used to differentiate the presence of **sufficient** and **insufficient collaterals**.

(e) Using collateral connections

Werner *et al.* (2003) devised another system of grading coronary collaterals and proposed a grading system based on collateral connections between the donor and the recipient vessels. The collateral connections were graded as follows:

Grade 0: collateral arteries showing no continuous connection between the donor and recipient arteries. This was referred to as CC0 (collateral connection grade 0) (Figure 33)

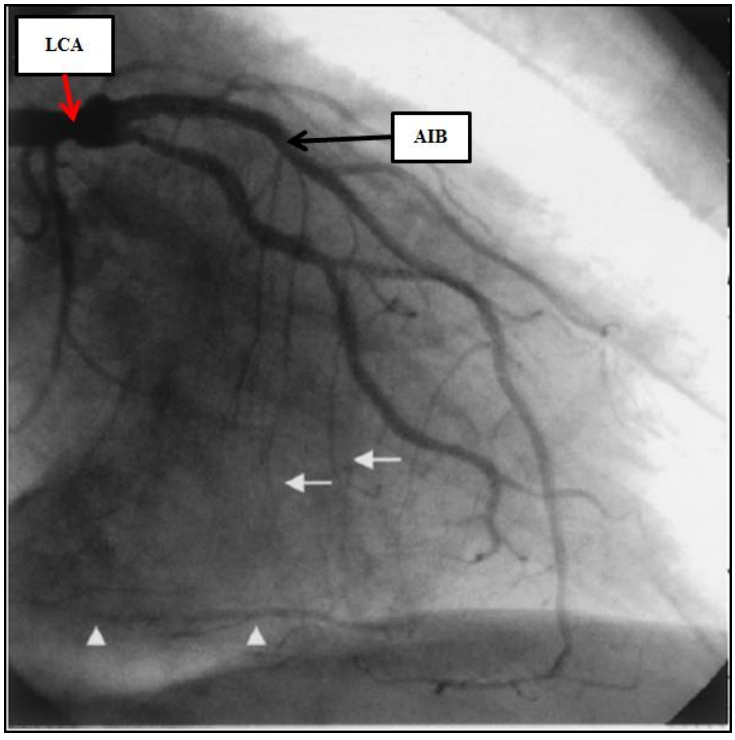

Figure 33: *Angiography of collateral connections in a patient with occluded RCA and filling of* posterior interventricular branch ***(arrowheads)*** *through septal branches from anterior interventricular branch with discontinuation of connections (**white arrows**: CC0) (Adapted from Werner et al., 2003)*

Key: **AIB**= anterior interventricular branch, **LCA**= left coronary artery

Grade 1: the presence of continuous threadlike connections between the donor and recipient arteries. This was referred to as CC1 (collateral connection grade 1) (Figure 34).

Grade 2: the presence of continuous connections between the donor and recipient arteries. The collateral artery also has small side branches throughout its course. This was referred to as CC2 (collateral connection grade 2) (Figure 34).

Their study also estimated the size of the collateral connections and a diameter of ≤ 0.3 mm was for *grade 1* connections and ≥ 0.4 mm for *grade 2* connections. In addition, the diameter of the collateral connections was correlated to the function of the vessels.

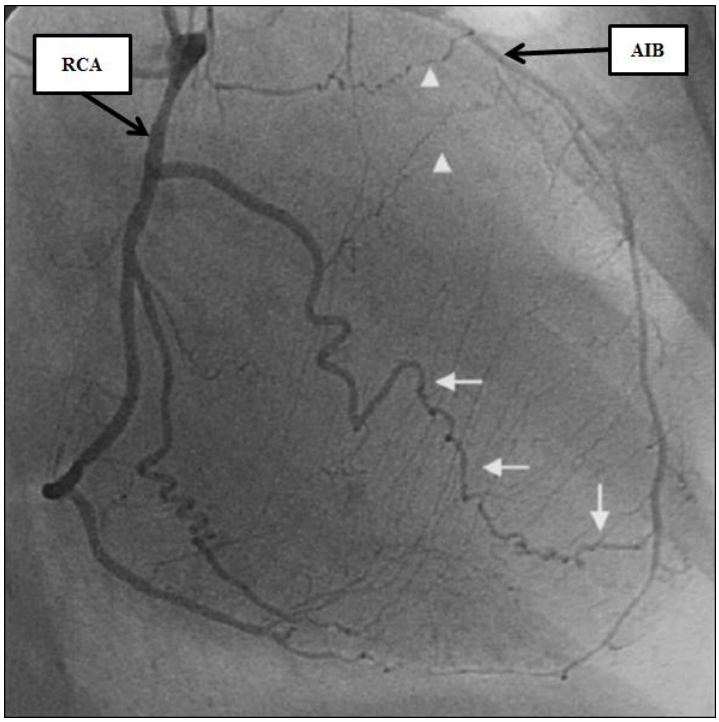

Figure 34: *Angiography of collateral connections in a patient with occluded proximal anterior interventricular branch collateralized from right ventricular branch of the RCA (white arrows: CC2) and additional septal and proximal connections (white arrowheads: CC1)*
(Adapted from Werner et al., 2003)

Key: **AIB**= anterior interventricular branch, **RCA**= right coronary artery

2.4.7 SHORTFALLS OF THE CURRENT CLASSIFICATION SYSTEMS

As noted earlier, it is apparent from the literature reviewed that Levin's (1974) report on coronary collateral pathways is the most extensive anatomic description of these pathways. In addition, in the various reports on the anatomic and functional grading of the coronary collaterals, the collateral vessels were evaluated using different methods and references. Furthermore, to date, there is no consensus on the method of assessing and reporting the coronary collateral vessels in patients with coronary arterial obstruction. Hence, it may be deduced that there is no unified system for the anatomic and functional classification of the coronary collateral pathways.

Consequently, this has resulted in conflicting results with respect to the anatomy, function and clinical significance of the coronary collateral pathways. From the literature reviewed, there appears to be no report that has evaluated the anatomic pathways and functional importance of the coronary collaterals in the same study. The lack of a unified system for coronary collateral vessels assessment has led to difficulty in communication amongst researchers and clinicians with respect to the significance of these vessels (Loukas *et al*., 2009a). Therefore, it is essential to have a system of coronary collateral artery evaluation that incorporates the anatomic and functional parameters of these vessels.

2.5 CLINICAL IMPORTANCE OF CORONARY COLLATERALS

Controversy has existed for decades with regard to the functional significance of coronary collaterals in humans (Traupe *et al*., 2010), and this has been compounded by the lack of a reference method for determining the coronary collateral flow in man (Wainwright *et al*., 1980; Baroldi *et al*., 2005). These collateral arteries are reported to have a protective effect on myocardial perfusion, contractile function (Heaps and Parker, 2011) and prevent left ventricular aneurysm formation (Hirai *et al*., 1989) in the presence of severe coronary artery obstruction. Coronary collaterals have also been documented to protect the ventricle from aneurysm formation in cases of unsuccessful reperfusion (Sasayama and Fujita, 1992). The presence of collateral vessels may play a major role in the determination of myocardial vulnerability and subsequent damage (Koerselman *et al*., 2003).

The use of coronary angiography has allowed the correlation of the anatomic appearance of the coronary collaterals with the severity of the coronary arterial disease (Gensisni and Bruto da Costa, 1969; Sasayama and Fujita, 1992). An adequately developed coronary collateral vasculature has been shown to have a protective role on the myocardium in cases of severe coronary artery occlusion (Meier *et al*., 2007). Meier *et al*., (2007) in their study concluded that "*A well-functioning coronary collateral circulation saves lives in patients with chronic stable coronary artery disease*". The presence of functional collateral vessels may be of good prognosis (Loukas *et al*., 2009a) and may also determine the need for surgical intervention such as coronary artery bypass graft (Levin *et al*., 1973). In addition, the development of a functional coronary collateral vasculature

has been correlated with relief of anginal pain in patients with coronary artery disease (Rockstroh and Brown, 2002).

Meier *et al*. (2013) in an analysis of previous studies on the effect of coronary collaterals on mortality reported that well developed collaterals reduced mortality by about 35%. The presence of adequately developed collateral supply limits the degree of MI during myocardial ischemia (Cohen and Rentrop, 1986; Sasayama and Fujtia, 1992). The area at risk of MI is inversely related to the collateral supply to that region, and therefore becomes zero in the presence of well-developed functional collaterals (de Marchi *et al*., 2005; Gloekler and Seiler, 2007; Choi *et al.*, 2013) (Figure 35).

In cases of unsuccessful intra-coronary thrombolytic therapy after the onset of symptoms in acute MI, the improvement in ventricular function and wall motion in the infarct region have been associated with the presence of collateral flow to the region perfused by the obstructed vessel (Schwartz *et al*., 1985; Hirai *et al*., 1989). Habib *et al*. (1991) recorded a higher ejection fraction before treatment and at discharge from hospital in patients with angiographically demonstrated collaterals than those without collaterals in acute MI.

There is an improvement in the success of coronary artery bypass graft surgery in the presence of good flow to the distal segment of an obstructed coronary artery by antegrade filling or collateral circulation or both. Although, the surgical significance of collateral circulation has not yet been properly investigated, it has been reported that the

preservation of left ventricular contractility and the patency of the distal segments of obstructed arteries by the collateral circulation is favorable for the successful construction of coronary artery bypass grafts (Levin 1974).

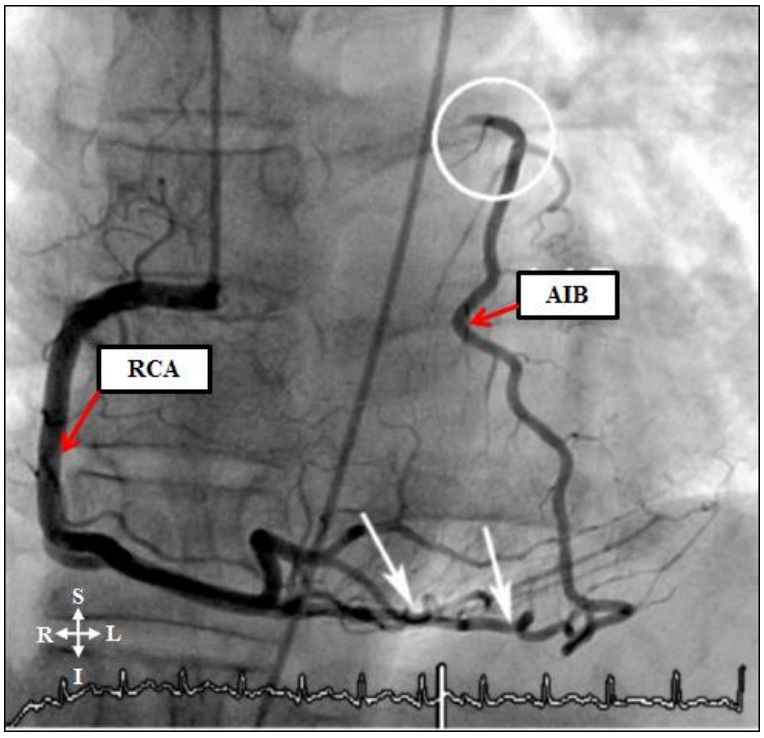

Figure 35: *Coronary angiogram showing the complete filling of the anterior interventricular branch obstructed at its origin (ring) from the posterior interventricular branch (white arrows) of the RCA*
(Adapted from Gloekler and Seiler, 2007)

Key: **AIB**= anterior interventricular branch, **RCA**= right coronary artery

Conversely, it has been reported that the preservation of left ventricular function do not differ in patients with or without good coronary collaterals. In addition, the incidence of left ventricular aneurysm formation was not lowered by the presence of coronary collaterals (Banerjee *et al*., 1993). Ilia *et al*. (1998) also reported that there was no difference in the characteristics of coronary collaterals in the presence or absence of left

ventricular systolic functional abnormality in patients with significant coronary artery disease. Furthermore, Turgut *et al*. (2009) stated that coronary collaterals do not have a protective role on left ventricular function preservation in the presence of severe anterior interventricular branch stenosis. It was also reported that the development of good coronary collaterals increased the risk of re-stenosis after percutaneous coronary intervention (Meier *et al*., 2012).

2.5.1 THERAPEUTIC POTENTIALS

Therapeutic arteriogenesis is part of the new approach for the development of collateral vessels (‘‘natural bypasses’’) for the revascularization of the myocardial tissue during ischaemia (Seiler, 2003). This approach has a prospect for clinical utility, especially in patients with refractory angina not suitable for revascularization, or in the desire to enlarge coronary collaterals to aid retrograde attempt at angioplasty in chronic total coronary occlusion (Ladwiniec and Hoye, 2013).

However, there are still gaps in the knowledge of coronary collateral growth (Chilian *et al*., 2012). So far, attempts at pharmacological stimulation of coronary collateral growth have been met with limited success (Ladwiniec and Hoye, 2013). Therefore, an adequate understanding of the detailed process and regulatory mechanism of arteriogenesis as opposed to vasculogenesis is necessary for designing such method of therapy (Seiler, 2003). Agents such as vascular endothelial growth factors and heparin have been used in the stimulation of arteriogenesis for developing coronary collaterals. These methods have been employed in the treatment of patients with occlusive coronary artery disease (van Royen *et al*., 2001).

2.5.2 RETROGRADE ANGIOPLASTY

Chronic total occlusion (CTO) of the coronary vessel is defined as an occlusion present for at least three months (Shah, 2011). It has been reported that re-opening of the occluded vessel improves patients' survival if the myocardial region supplied by the vessel is still viable (Valenti *et al*., 2008; Hsu *et al*., 2009). Traditionally, the anterograde approach was used to get to the point of occlusion. In recent times, different Japanese groups (Saito, 2008; Rathore *et al*., 2009a) have innovated and perfected the retrograde approach to the point of occlusion in the affected vessel via coronary collaterals from an unobstructed coronary artery (Ozawa, 2006; Fernández-Díaz *et al*., 2010). The method is intricate; however, some groups have reported a success rate of about 90% (Rathore *et al*., 2009b).

The retrograde access to the point of occlusion was initially introduced via bypass graft (Khan *et al*., 1990) and later through epicardial collaterals (Sumerly *et al*., 2007). However, the preferred route is through the septal collaterals because of their intramuscular course which is safer than the epicardial collaterals in case of vessel perforation (Sumerly *et al*., 2007; Fernández-Díaz *et al*., 2010). Due to the high success rate achieved using this technique, the retrograde approach is regarded as a safe and effective procedure in CTO management (Fernández-Díaz *et al*., 2010).

CHAPTER 3

MATERIALS AND METHODS

3.1 MATERIALS

3.1.1 REVIEWED CORONARY ANGIOGRAMS

The study group was selected from the retrospectively reviewed angiographic records of consecutive patients (n= 2029) (mean age: 59 ± 12 years) that had coronary catheterization performed by interventional Cardiologists for symptoms suggestive of coronary artery disease. The patients consisted of 37.1% ($^{753}/_{2029}$) females (mean age: 61 ± 11 years) and 62.9% ($^{1276}/_{2029}$) males (mean age: 57 ± 12 years). The angiograms were obtained from the cardiac catheterization laboratories of hospitals within the private sector in the eThekwini Municipality region of KwaZulu-Natal, South Africa. Ethical approval (Ethics number BE 196/13) for the study was obtained from the University of KwaZulu- Natal Biomedical Research Ethics Committee.

Coronary arteriography was performed via the percutaneous trans-femoral approach by injecting radio-opaque contrast agent into the coronary blood vessels and the images were obtained by using fluoroscopic method. These images were recorded on digital media in DICOM (Digital Imaging and Communication in Medicine) format and stored in the cardiac catheterization laboratories.

3.1.2 SELECTED CORONARY ANGIOGRAMS

Of the coronary angiograms reviewed (n=2029), the coronary angiograms of the patients (n=286) (mean age: 59 ± 11 years) that met the inclusion criteria for the study were selected for analysis.

Inclusion Criteria

The coronary angiograms with the total obstruction of any of the following coronary arteries: LCA, RCA anterior interventricular branch, circumflex branch and their branches.

Exclusion Criteria

Criteria for exclusion were: i) patients without total obstruction of any of the main coronary arteries or their branches; ii) patients who already had coronary artery bypass surgery, coronary stent placement and/or coronary angioplasty; iii) coronary angiograms with unsatisfactory visualization of the coronary arteries or poor images.

3.2 METHODS

Coronary angiograms with the presence of total obstruction of the coronary arteries were analyzed using Phillips DICOM viewer 3.0 software. These angiograms were examined in the LAO, RAO and lateral projections with various degrees of cranial and caudal angulations. The coronary collateral pathways formed in these angiograms were observed and documented. All the connections within the same vessel and between different vessels were documented, grouped and classified. The influence of the patients' sex and age (divided into two age group which are ≤ 60 years and > 60 years based on the patients' mean age) on the development of the collaterals was examined. The coronary collateral pathways were shown with "plates" in the result section of this dissertation. Ideally, each collateral pathway would have been represented with a plate, however, because the plates were obtained from fluoroscopic images, only the images with clearly shown collateral pathways were included.

The following morphologic parameters were documented:-

- Branching patterns of the LCA
- Coronary arterial dominance
- Location of the coronary arterial obstruction
- Origin and termination of collateral arteries
- Direction of flow of the coronary collateral vessel
- Non-coronary collateral vessels (if present)

3.2.1 CORONARY ARTERIAL SEGMENTATION

The location of coronary arterial obstruction, origin and termination of collateral arteries were identified and documented by dividing the coronary arterial tree into segments using the BARI coronary arterial map (Figure 20; Image repeated below for ease of reference).

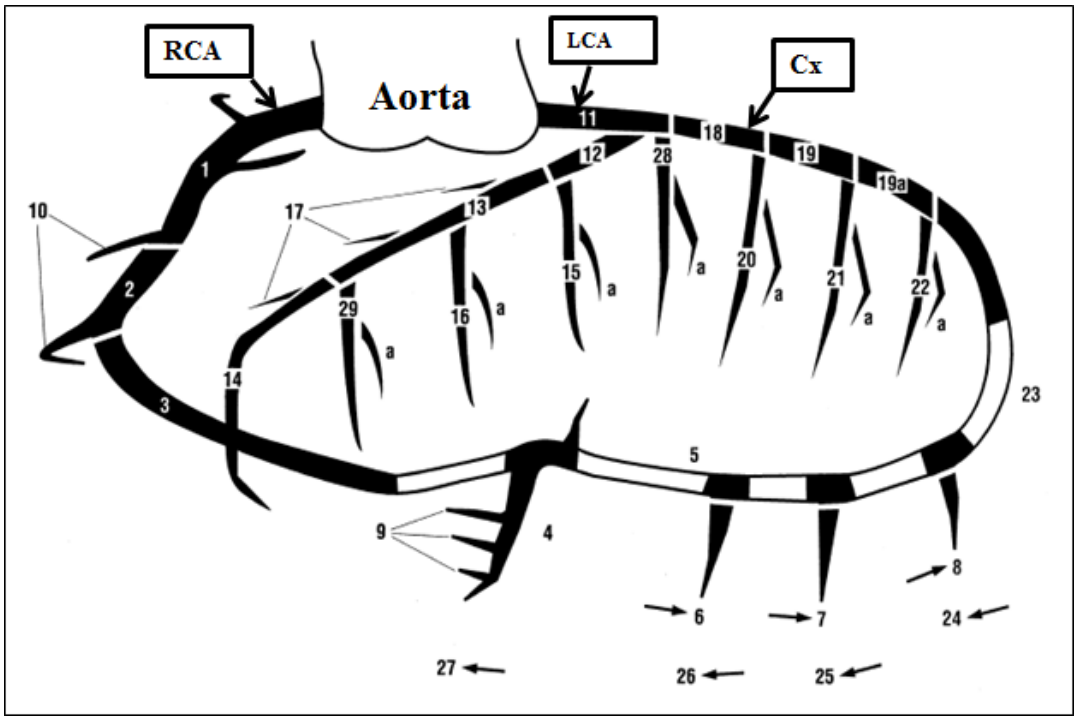

Figure 20: *The Bypass Angioplasty Revascularization Investigation coronary artery map. Right coronary artery:* ***1****-proximal;* ***2****-middle;* ***3****-distal;* ***4****-posterior interventricular branch;* ***5****-right posteroatrioventricular;* ***6****-first posterolateral;* ***7****-second posterolateral;* ***8****-third posterolateral;* ***9****-inferior septal artery;* ***10****- right margina artery. Left coronary artery:* ***11****-left main;* ***12****-proximal anterior interventricular branch;* ***13****-middle anterior interventricular branch;* ***14****-distal anterior interventricular branch;* ***15****-first diagonal;* ***15a****-first diagonal branch;* ***16****-second diagonal;* ***16a****-second diagonal branch;* ***17****-anterior septals;* ***18****-proximal circumflex;* ***19****-middle circumflex;* ***19a****-distal circumflex;* ***20, 21, 22****- first, second and third left marginal;* ***20a, 21a, 22a****-first, second and third left marginal branches;* ***23****-left atrioventricular;* ***24, 25, 26****-first, second and third posterolaterals;* ***27****-left posterior interventricular branch;* ***28****-Ramus;* ***28a****-Ramus branch;* ***29****-third diagonal;* ***29a****-third diagonal branch*
(Adapted from Alderman and Stadius, 1992).

Key: **LCA**- Left Coronary Artery; **RCA**- Right Coronary Artery; **Cx**- Circumflex branch.

In addition, in the present study, the segments of the coronary arteries (anterior interventricular branch, circumflex branch and RCA) were also grouped into three main regions viz. proximal, middle and distal regions of each vessel (Figure 36) as follows:-

(a) Right coronary artery

Proximal region – Segment 1, *Middle region*- Segments 2 and 10, and *Distal region*- Segments 3, 4 and (when present) 5, 6, 7 and 8.

(b) Anterior interventricular branch

Proximal region– Segments 12, 15 and 15a, *Middle region* - Segments 13, 16, 16a and 29, and *Distal region* - Segment 14.

(c) Circumflex branch

Proximal region – Segments 18 and 20, *Middle region* - Segments 19 and 21, and *Distal region* - Segments 19a, 22 and (when present) 23, 24, 25 and 26.

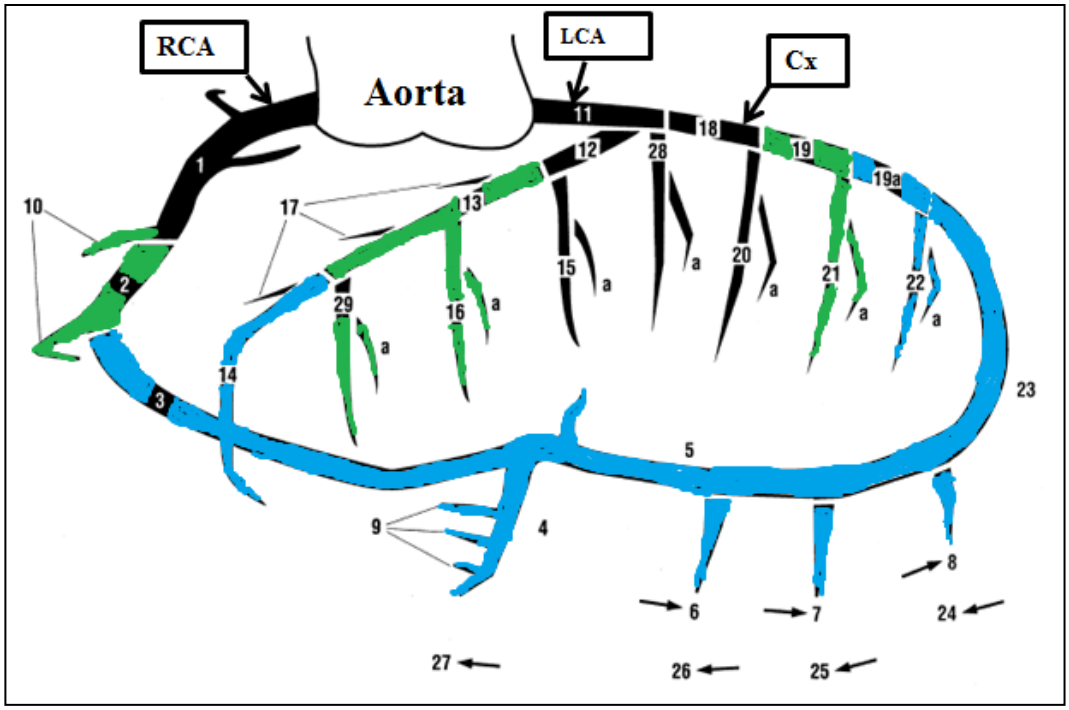

Figure 36: *Division of the Bypass Angioplasty Revascularization Investigation coronary artery map into regions. Proximal regions of the anterior interventricular branch, circumflex branch and RCA (Colour coded black), middle regions of the anterior interventricular branch, circumflex branch and RCA (Colour coded green), distal regions of the anterior interventricular branch, circumflex branch and RCA (Colour coded blue)*

Key: **LCA**- Left Coronary Artery; **RCA**- Right Coronary Artery; **Cx**- Circumflex branch.

3.2.2 GRADING OF STENOTIC LESIONS

As noted earlier, the coronary angiograms selected for analysis are those with total coronary artery obstruction. From a hemodynamic viewpoint, the presence of coronary arterial stenosis of between 75% and 90% produce moderate myocardial ischemia and anginal pain, therefore, they are not practically accompanied by angiographically detectable collateral circulation (Levin *et al*., 1974). In addition, functional coronary collaterals are better shown in coronary arterial obstruction than in high-grade coronary

arterial stenosis (Trappe *et al*., 1989). Clinically, angiographic method of coronary collateral grading remains the standard reference (Fujita *et al*., 1999).

The severity of coronary stenosis was evaluated in the present study using the method designed by the BARI study group (Alderman and Stadius, 1992). In their study, the severity of coronary stenosis was determined by a combination of continuous scale and discrete categories. The continuous scale ranged from 1% to 90%, while the discrete categories were for 95%, 99% and 100% stenosis. The BARI study group defined the discrete group as follows:

Ninety-five percent stenosis: Severe lesion in which the contrast column, though visible within the lesion, is so narrow and faint that reproducible measurement using caliper is extremely difficult.

Ninety-nine percent stenosis: Severe lesion in which there is anterograde flow of the contrast, however, the contrast column through the lesion is not visible and therefore cannot be measured by caliper.

One hundred percent stenosis: corresponds to total vessel obstruction

3.2.3 TYPES OF OBSTRUCTIVE VESSEL DISEASE

The presence of obstructive atherosclerotic lesions in main coronary arteries such as the RCA, anterior interventricular branch or circumflex branch in the angiograms analyzed was regarded as *single*, *double* and *triple vessel obstructive coronary artery disease.* The angiograms were recorded as *single*, *double* and *triple vessel obstructive coronary artery disease* when *one*, *two* or *all three* of these vessels were obstructed, respectively.

3.2.4 GRADING OF CORONARY COLLATERALS

The Rentrop grading system (Rentrop *et al*., 1985) is the most widely used grading system for coronary collaterals by most researchers. However, this system has been reported not to be very useful in patients with total coronary occlusion (van der Hoeven *et al.,* 2013). The grading of the functional capacity of the coronary collaterals in the present study was based on the grading system used by Werner *et al*. (2003) (Page 56). This system centered on the collateral connection between the donor and the recipient arteries. In addition, this grading of collaterals is applicable during diagnostic angiography and was shown to have a close association with clinical determinants of collateral adequacy (Werner *et al*. 2003). Therefore, in the present study, Werner *et al*.'s (2003) grading of the coronary collateral connections was modified by the addition of a grade for absent coronary collaterals and the coronary collaterals were graded as:

Grade 0 (***absent*** collateralization): no collaterals to the distal region of the obstructed vessel

Grade 1 (***poor*** collateralization): collateral arteries showing no continuous connection between the donor and recipient arteries

Grade 2 (***good*** collateralization): the presence of continuous threadlike connections between the donor and recipient arteries

Grade 3 (***excellent*** collateralization): the presence of continuous prominent connections with side branches between the donor and recipient arteries

3.2.5 PROPOSED ALGORITHM FOR LABELLING CORONARY COLLATERALS

Using the BARI coronary segments, an algorithm is proposed in the present study for the labelling of the coronary collaterals. It incorporates the vessel(s) occluded by atherosclerotic lesion(s), the presence or absence of coronary collateral(s) to the distal segment of the occluded vessel, origin and termination of the coronary collaterals (when present) and the grading of the coronary collaterals (Figure 37).

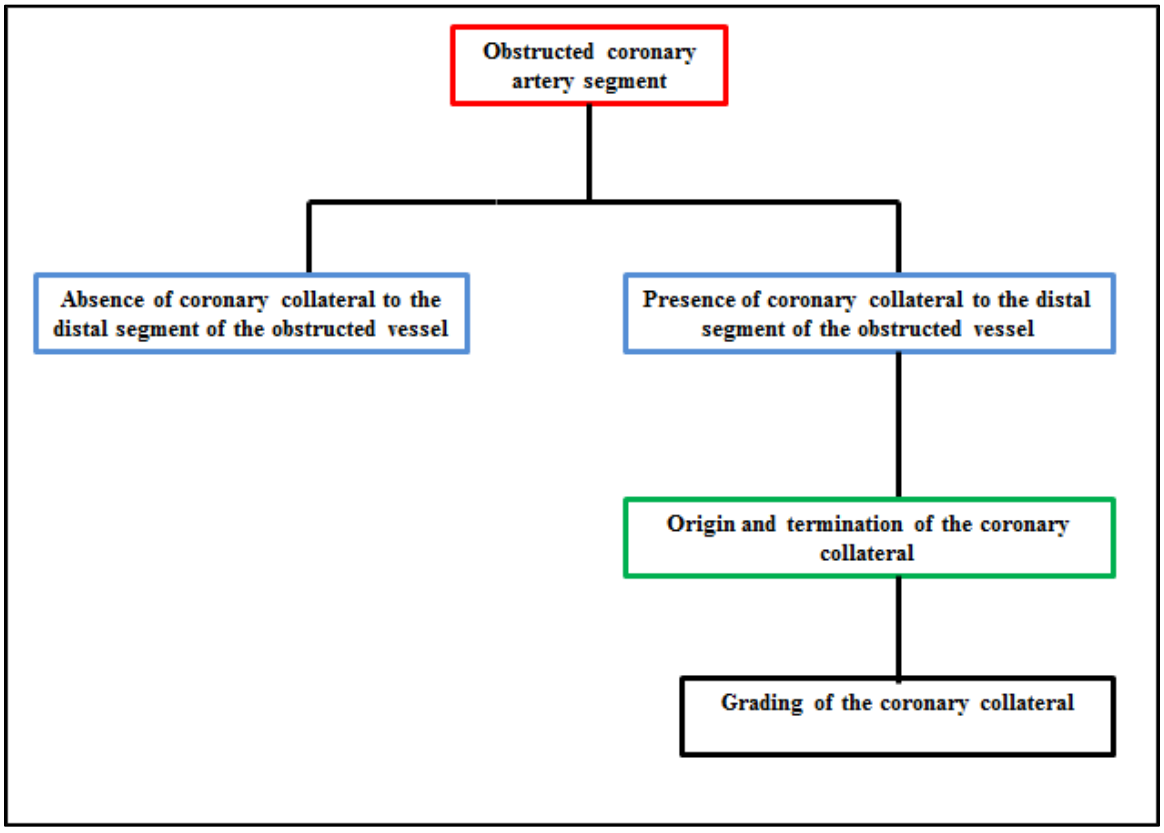

***Figure 37**: Proposed algorithm for coronary collateral arterial classification.* ***First step (Red box)**: Identify the obstructed vessel and the segment involved.* ***Second step (Blue boxes)**: Identify the presence or absence of coronary collaterals.* ***Third step (Green box)**: Determine the coronary artery segments of origin and termination of the coronary collateral vessel.* ***Fourth step (Black box)**: Determine the grade of the collateral vessel.*

3.2.6 EFFECT OF CORONARY COLLATERAL ARTERIES ON LEFT VENTRICULAR FUNCTION

In order to assess the effect of coronary collateral arteries on left ventricular function in the presence of total obstruction of the coronary arteries, the coronary angiograms of the patients that had their left ventricle assessed with ventriculography were selected for analysis. Ninety-seven (n=97) patients with total obstruction of any of the coronary arteries had left ventricular function assessed, and the mean ejection fraction (EF) of these patients with the different grades of coronary collaterals was compared. The relationship between the location of atherosclerotic lesions and the coronary collateral grades was examined. In addition, the relationship between the location of atherosclerotic lesions and the mean EF was also evaluated.

3.3 STATISTICAL ANALYSIS

Data were entered into Statistical Package for the Social Sciences (SPSS) version 21 for Windows (IBM SPSS, NY, USA). A p value < 0.05 was considered as statistically significant. Data analysis was initiated with a check of the data for outliers, missing data and normality through skewness and kurtotis values that could affect relations between variables. A descriptive statistical analysis of the data (means, standard deviations, ranges, frequencies and percentages, etc.) was initially conducted prior to conducting inferential and multivariate analyses. The branching patterns, division and coronary arterial dominance were presented with descriptive analysis.

In consultation with a biostatistician, Pearson's Chi square test of association was used to evaluate the relationship between age and sex, location of atherosclerotic lesions, branching pattern of the coronary arteries and the development of the coronary collateral pathways. The Analysis of Variance (ANOVA) test was used to determine the difference in the mean EF between the grades of coronary collaterals. Spearman's rho correlation analysis was used to evaluate the correlation between the development of coronary collateral pathways and left ventricular function in the presence of coronary artery obstruction.

CHAPTER 4

RESULTS

4.1 SAMPLE DISTRIBUTION

Of the coronary angiograms reviewed (n=2029), the coronary angiograms of the patients (n=286) that met the inclusion criteria were selected for analysis. The sex distribution of these patients was 21.7% ($^{62}/_{286}$) females and 78.3% ($^{224}/_{286}$) males and the mean age was 59 ± 11 years (range 29 – 93 years). The mean age for females and males were 64 years ± 11 (range 42 – 93 years) and 57 ± 10 years (range 29 – 87 years), respectively. The mean age calculated for females was significantly higher than the mean age for males ($p < 0.001$).

4.2 MORPHOLOGIC ANALYSIS

The LCA divided into its terminal branches by 3 different branching patterns which are recorded as bifurcation 91% ($^{260}/_{286}$), trifurcation 8.7% ($^{25}/_{286}$) and quadrifurcation 0.3% ($^{1}/_{286}$). Three types of coronary arterial dominant patterns were observed in the coronary angiograms viz. right 82.9% ($^{237}/_{286}$), left 13.6% ($^{39}/_{286}$) and co-dominance 3.5% ($^{10}/_{286}$).

4.3 DISTRIBUTION OF OBSTRUCTIVE ATHEROSCLEROTIC LESIONS

The presence of obstructive atherosclerotic lesions in the main coronary arteries (anterior interventricular branch, circumflex branch and RCA) resulting in single, double and triple vessel obstructive disease patterns were recorded in 86% ($^{246}/_{286}$), 12.9% ($^{37}/_{286}$) and 1% ($^{3}/_{195}$) of the angiograms analyzed, respectively. Therefore, a total of n=329 coronary arterial total obstructions were recorded in the angiograms analyzed, and these obstructions were found in the main coronary arteries as follows: anterior interventricular branch -*76* obstructions, circumflex branch -*87* obstructions and RCA -*166* obstructions.

4.3.1 ANTERIOR INTERVENTRICULAR ARTERY

Atherosclerotic lesions resulting in total obstruction of the anterior interventricular branch was recorded in 76 of the coronary angiograms analyzed.

(a) Type of obstructive vessel disease

Single obstructive vessel disease of the anterior interventricular branch in which it was obstructed in any of its segments was present in 69.7% ($^{53}/_{76}$) of the angiograms analyzed, while double (with another main coronary artery) and triple (with two other main coronary arteries) obstructive vessel disease involving the anterior interventricular branch were recorded in 26.3% ($^{20}/_{76}$) and 3.9% ($^{3}/_{76}$) of the angiograms analyzed, respectively (Figure 38).

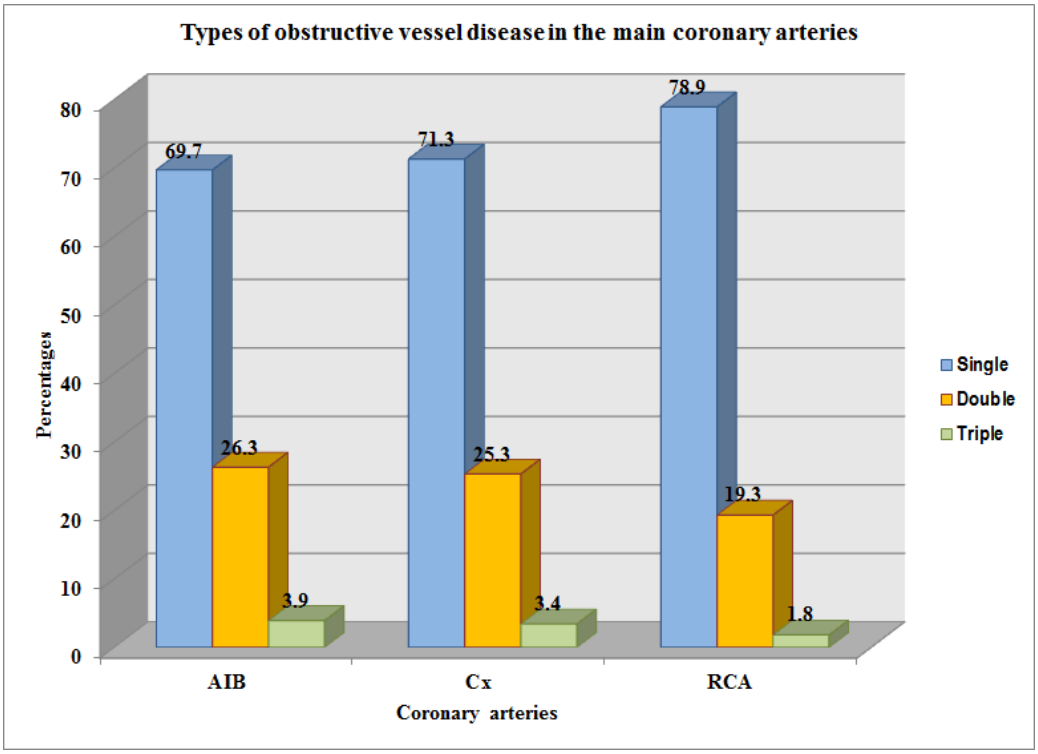

***Figure 38**: Types of obstructive vessel disease in the main coronary arteries*

Key: **RCA** = right coronary artery, **Cx**= circumflex branch, **AIB** = anterior interventricular branch

(b) Location of atherosclerotic lesions in the anterior interventricular branch

The location of the obstructive atherosclerotic lesions in the segments of the anterior interventricular branch were recorded as 52.6% ($^{40}/_{76}$), 30.3% ($^{23}/_{76}$), 2.6% ($^{2}/_{76}$), 10.5% ($^{8}/_{76}$) and 3.9% ($^{3}/_{76}$) for segments 12, 13, 14, 15 and 16, respectively. Therefore, the atherosclerotic lesions were found in the *proximal*, *middle* and *distal regions* of the anterior interventricular branch in 63.2% ($^{48}/_{76}$), 34.2% ($^{26}/_{76}$) and 2.6% ($^{2}/_{76}$) of these angiograms, respectively (Figure 39).

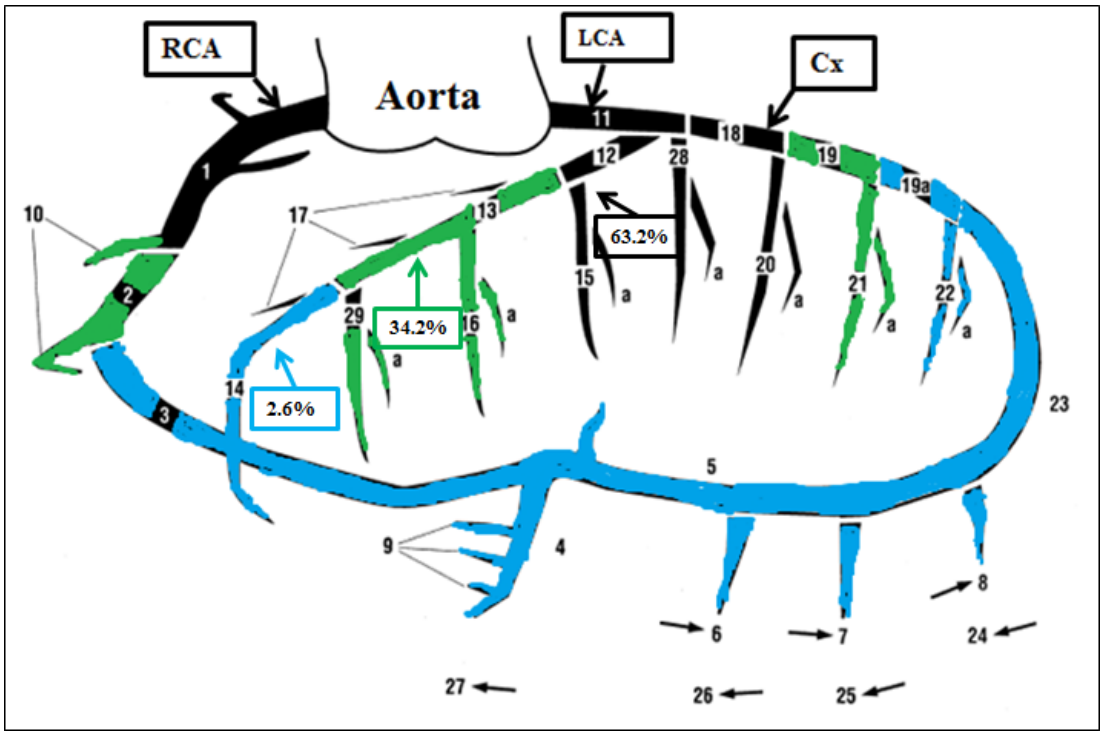

Figure 39*: Distribution of atherosclerotic lesions in the proximal, middle and distal regions of the anterior interventricular branch using the BARI coronary map*

Key: **LCA** = left coronary artery, **RCA** = right coronary artery, **Cx**= circumflex branch

4.3.2 CIRCUMFLEX BRANCH

Atherosclerotic lesions resulting in total obstruction of the circumflex branch was recorded in 87 of the coronary angiograms analyzed.

(a) Type of obstructive vessel disease

Single obstructive vessel disease of the circumflex branch was present in 71.3% ($^{62}/_{87}$) of the angiograms analyzed, while double (with another main coronary artery) and triple (with two other main coronary arteries) obstructive vessel disease involving the circumflex branch were recorded in 25.3% ($^{22}/_{87}$) and 3.4% ($^{3}/_{87}$) of the angiograms analyzed, respectively (Figure 38).

(b) Location of atherosclerotic lesions in the circumflex branch

The location of the obstructive atherosclerotic lesions in the segments of the circumflex branch were recorded as 34.5% ($^{30}/_{87}$), 26.4% ($^{22}/_{87}$), 12.6% ($^{11}/_{87}$), 11.5% ($^{10}/_{87}$), 8% ($^{7}/_{87}$) and 6.9% ($^{6}/_{87}$) for segments 18, 19, 19a, 20, 21 and 23, respectively. Therefore, the atherosclerotic lesions were found in the *proximal, middle* and *distal regions* (Figure 36; Page 69) of the circumflex branch in 46% ($^{40}/_{87}$), 34.5% ($^{30}/_{87}$) and 19.5% ($^{17}/_{87}$) of these angiograms, respectively (Figure 40).

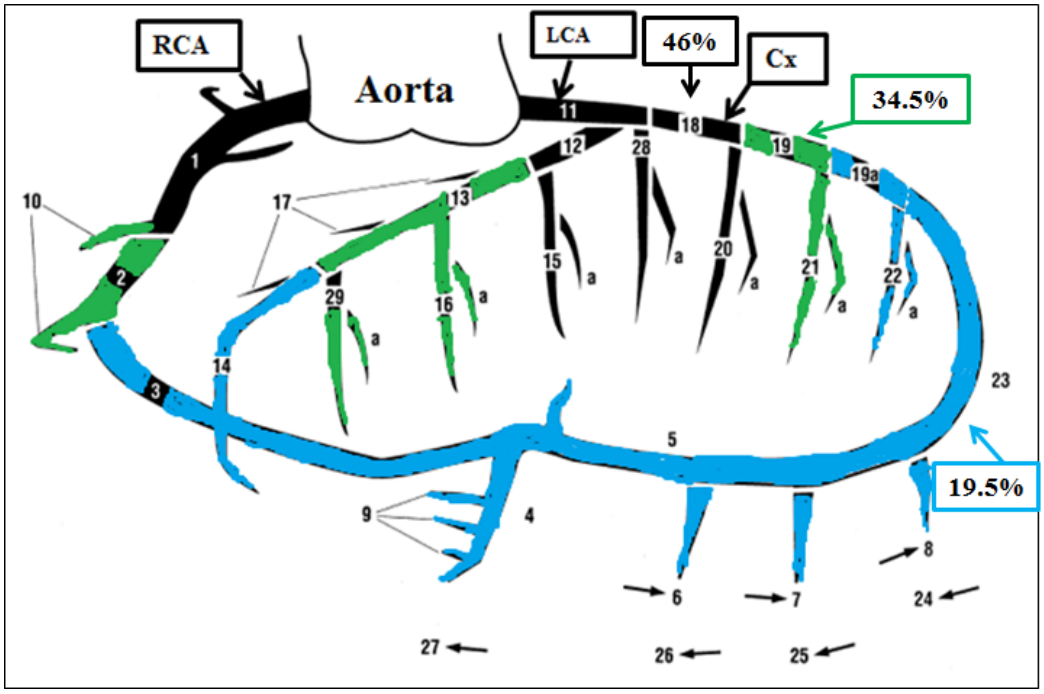

***Figure 40**: Distribution of atherosclerotic lesions in the proximal, middle and distal regions of the circumflex branch using the BARI coronary map*

Key: **LCA** = left coronary artery**, RCA** = right coronary artery, **Cx**= circumflex branch

4.3.3 RIGHT CORONARY ARTERY

Atherosclerotic lesions resulting in total obstruction of the RCA was recorded in 166 of the coronary angiograms analyzed.

(a) Type of obstructive vessel disease

Single obstructive vessel disease of the RCA was present in 78.9% ($^{131}/_{166}$) of the angiograms analyzed, while double (with another main coronary artery) and triple (with two other main coronary arteries) obstructive vessel disease involving the RCA were recorded in 19.3% ($^{32}/_{166}$) and 1.8% ($^{3}/_{166}$) of these angiograms, respectively (Figure 38).

(b) Location of atherosclerotic lesions in the RCA

The location of the obstructive atherosclerotic lesions in the segments of the RCA were recorded as 41.6% ($^{69}/_{166}$), 39.2% ($^{65}/_{166}$), 12% ($^{20}/_{166}$), 6% ($^{10}/_{166}$) and 1.2% ($^{2}/_{166}$) for segments 1, 2, 3, 4 and 5, respectively. Therefore, the atherosclerotic lesions were found in the *proximal*, *middle* and *distal regions* (Figure 36; Page 69) of the RCA in 41.6% ($^{69}/_{166}$), 39.2% ($^{65}/_{166}$) and 19.2% ($^{32}/_{166}$) of these angiograms, respectively (Figure 41).

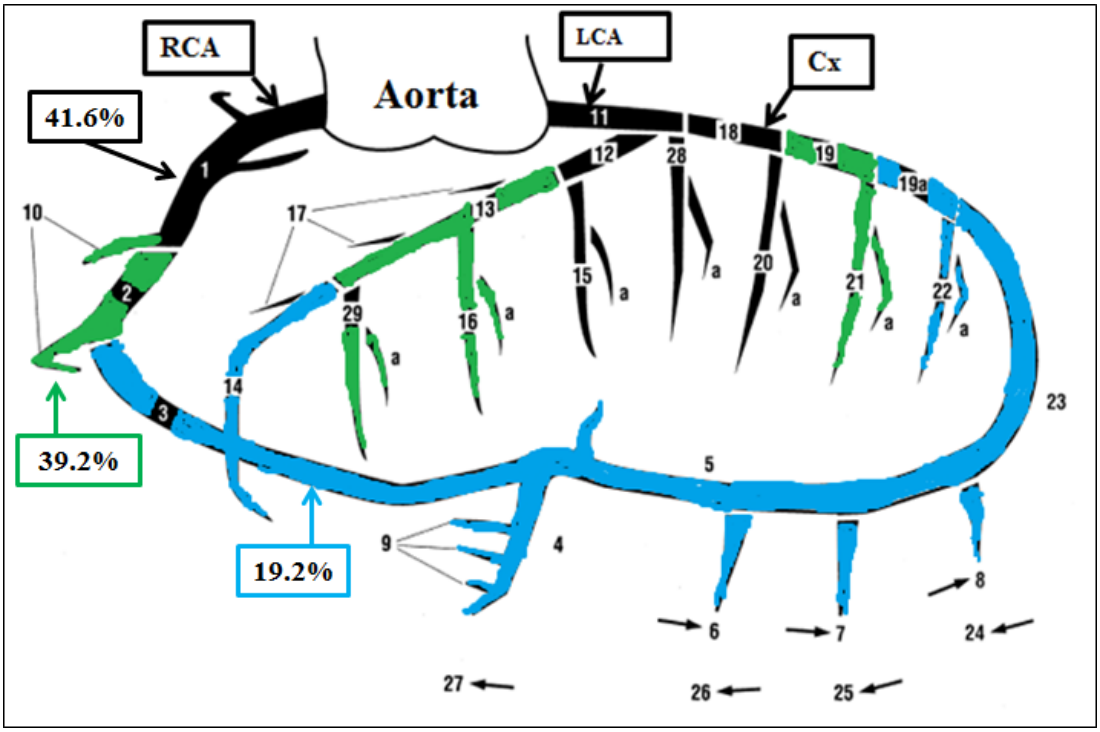

Figure 41*: Distribution of atherosclerotic lesions in the proximal, middle and distal regions of the RCA using the BARI coronary map*

Key: **LCA** = left coronary artery**, RCA** = right coronary artery, **Cx**= circumflex branch

4.4 ANATOMIC PATHWAYS OF CORONARY COLLATERALS IN TOTAL CORONARY ARTERIAL OBSTRUCTIONS

4.4.1 THE ANTERIOR INTERVENTRICULAR BRANCH

The total obstruction of the anterior interventricular branch (in any of its segments) was recorded in 76 of the coronary angiograms analyzed. In some of the angiograms with total obstruction of the anterior interventricular branch, there were no coronary collaterals to the distal segment(s) of the anterior interventricular branch or its branches. In some of the obstructions, there were more than one coronary collateral pathway and certain pathways occurred in more than one coronary angiogram.

(i) Segment 12

In the angiograms with total obstruction of the anterior interventricular branch, *segment 12* of the anterior interventricular branch was totally obstructed in 40 coronary angiograms. Coronary collaterals were absent in 10 of these angiograms and 40 collateral pathways were recorded in the remaining 30 coronary angiograms with collaterals to the anterior interventricular branch (Table 2; Plates 1-6).

***Table 2**: Coronary collateral pathways in the total obstruction of segment 12 (Figure 21) of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	23	14	1
2	9	17	8
3	20	14	3
4	28	14	1
5	4	17	1
6	21	13	1
7	17	13	1
8	Right ventricular branch	13	3
9	12	13	1
10	4	12	1
11	9	12	1
12	10	14	1
13	Right ventricular branch	14	4
14	9	14	2
15	10	13	1
16	28	13	1
17	15	13	2
18	4	14	2
19	Right conal branch	12	2
20	21	4	1
21	17	12	1
22	27	14	1
			40

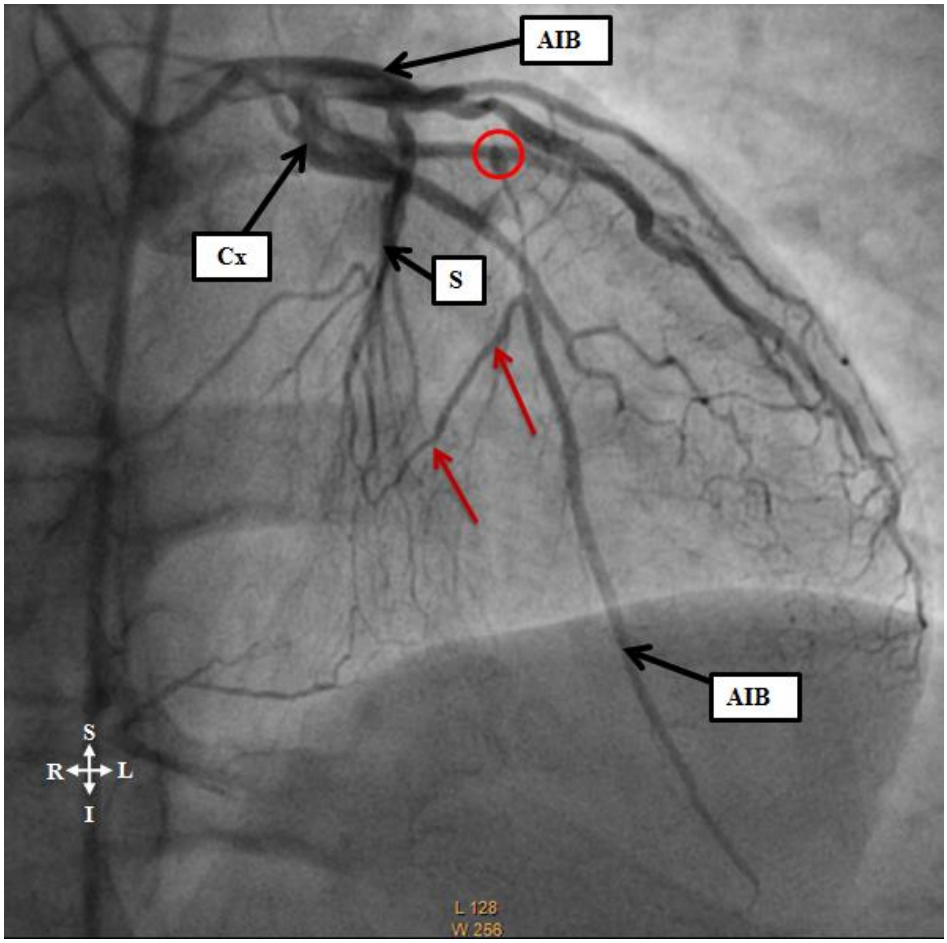

Plate 1: *Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment (red ring) by collateral vessel (red arrows) originating from segment 17(septal artery) and terminating at segment 13 of the anterior interventricular branch*

Key: **Cx**=circumflex branch, **AIB**=anterior interventricular branch, **S**=septal branch of anterior interventricular branch

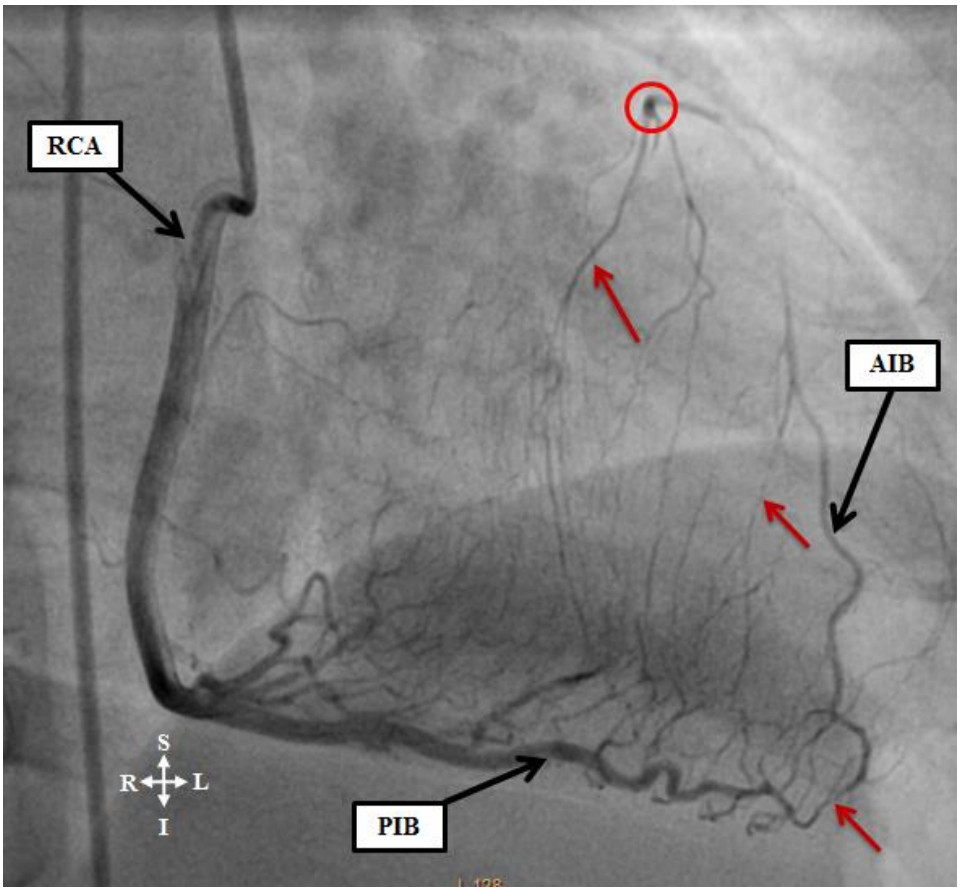

Plate 2: *Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment (red ring) by collateral vessels (red arrows) originating from segment 9 (septal of* posterior interventricular branch*) and segment 4 (posterior interventricular branch) and terminating at segments 13 and 14 of the anterior interventricular branch*

Key: **RCA**= right coronary artery, **AIB**= anterior interventricular branch, **PIB**= posterior interventricular branch

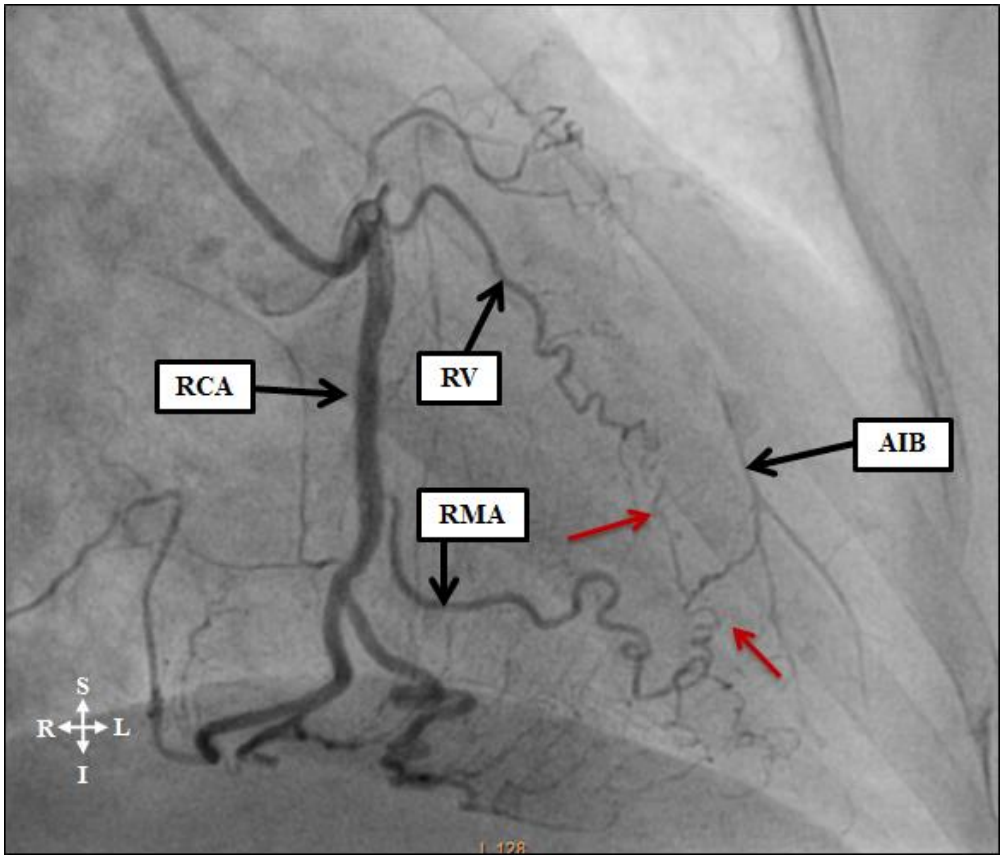

Plate 3: *Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment by collateral vessel (red arrows) originating from RV and right marginal artery (segment 10) branches RCA and terminating at segment 14 of the anterior interventricular branch*

Key: **RCA**=right coronary artery, **AIB**=anterior interventricular branch, **RMA**= right marginal artery, **RV**=right ventricular

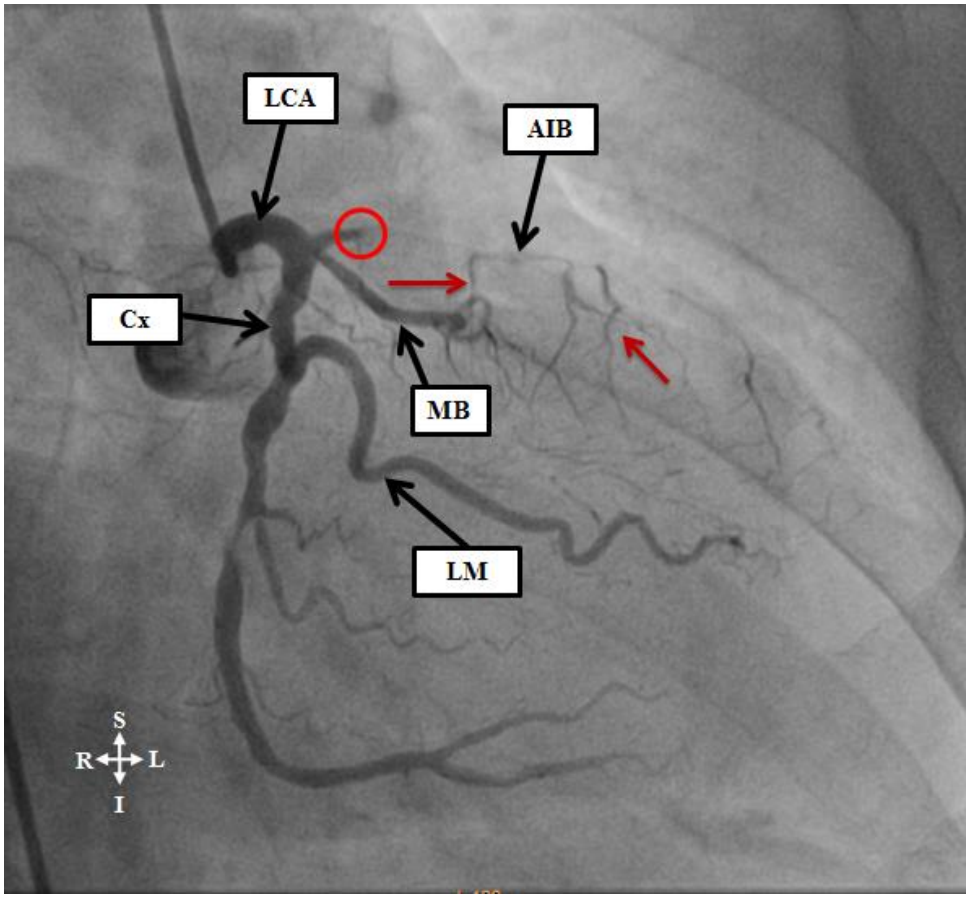

Plate 4: *Coronary angiogram in the RAO view showing the poor filling of the anterior interventricular branch obstructed at its proximal segment (red ring) by collateral vessel (red arrows) originating from segment 28 (MB) and terminating at segment 13 of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **MB**= median branch, **LM**=left marginal

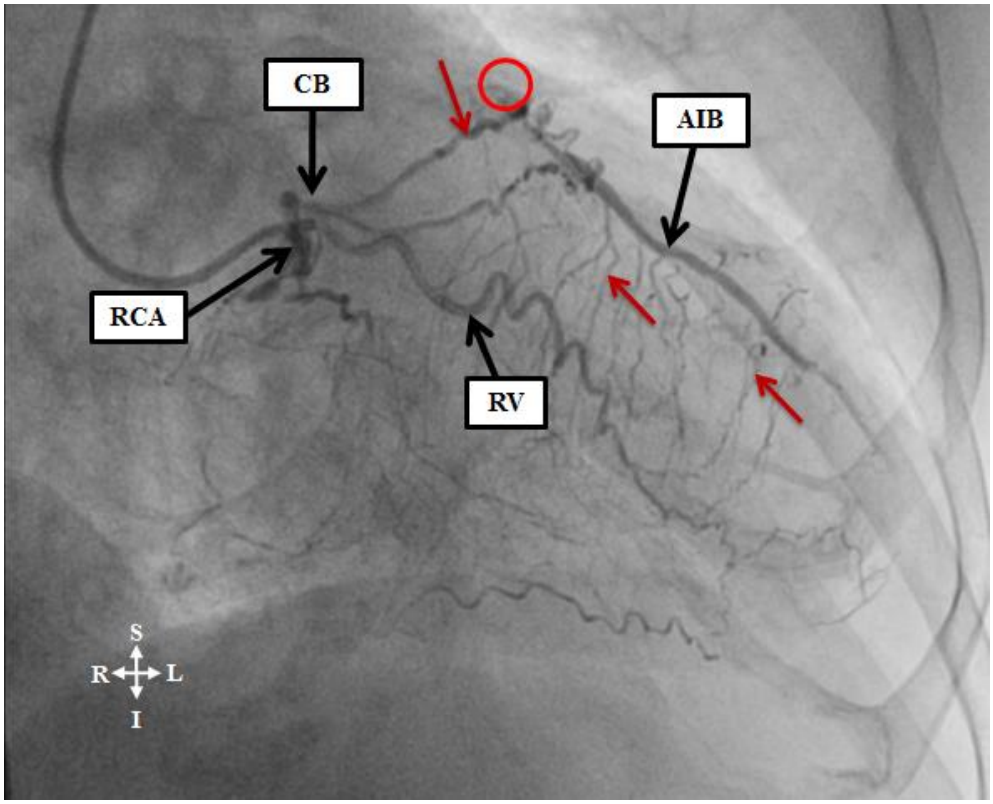

Plate 5: *Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment (red ring) by collateral vessels (red arrows) originating from the CB and RV of RCA (also obstructed) and terminating at segments 12 and 13 of the anterior interventricular branch*

Key: **RCA**=right coronary artery, **AIB**=anterior interventricular branch, **CB**=conal branch, **RV**=right ventricular branch

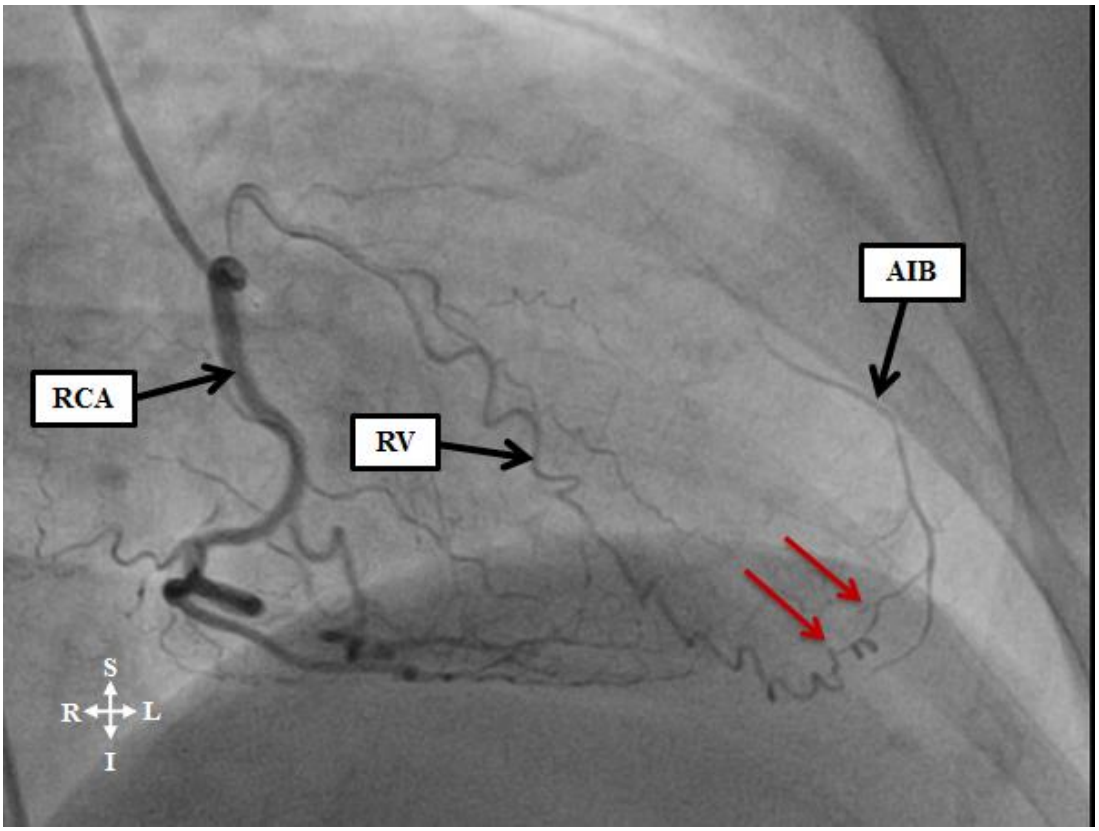

Plate 6: *Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment by collateral vessel (red arrows) originating from the RV of RCA and terminating at segment 14 of the anterior interventricular branch*

Key: **RCA**=right coronary artery, **AIB**=anterior interventricular branch, **RV**=right ventricular branch

(ii) Segment 13

In the angiograms with total obstruction of the anterior interventricular branch, *segment 13* of the anterior interventricular branch was totally obstructed in 23 coronary angiograms. Fifteen collateral pathways were recorded in 13 of these coronary angiograms with collaterals to the anterior interventricular branch (Table 3; Plates 7-9).

***Table 3**: Coronary collateral pathways in the total obstruction of segment 13 of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	17	17	2
2	13	13	4
3	17	13	2
4	12	13	2
5	4	14	1
6	15	16	1
7	9	13	2
8	20	14	1
			15

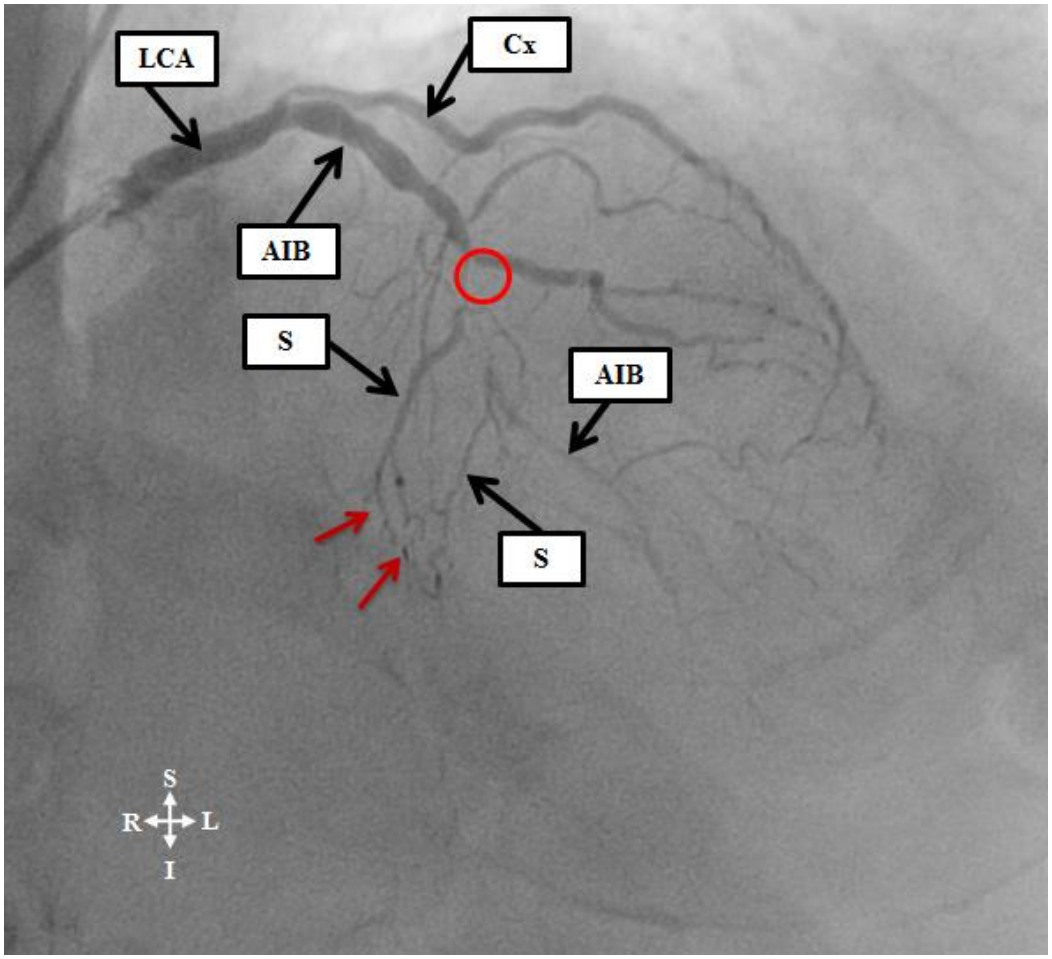

Plate 7: *Coronary angiogram in the RAO view (cranial angulation) showing the filling of the distal segment of the anterior interventricular branch obstructed at its mid- segment (red ring) by collateral vessels (red arrows) between the septal branches (segment 17) of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **S**=septal branch of anterior interventricular branch

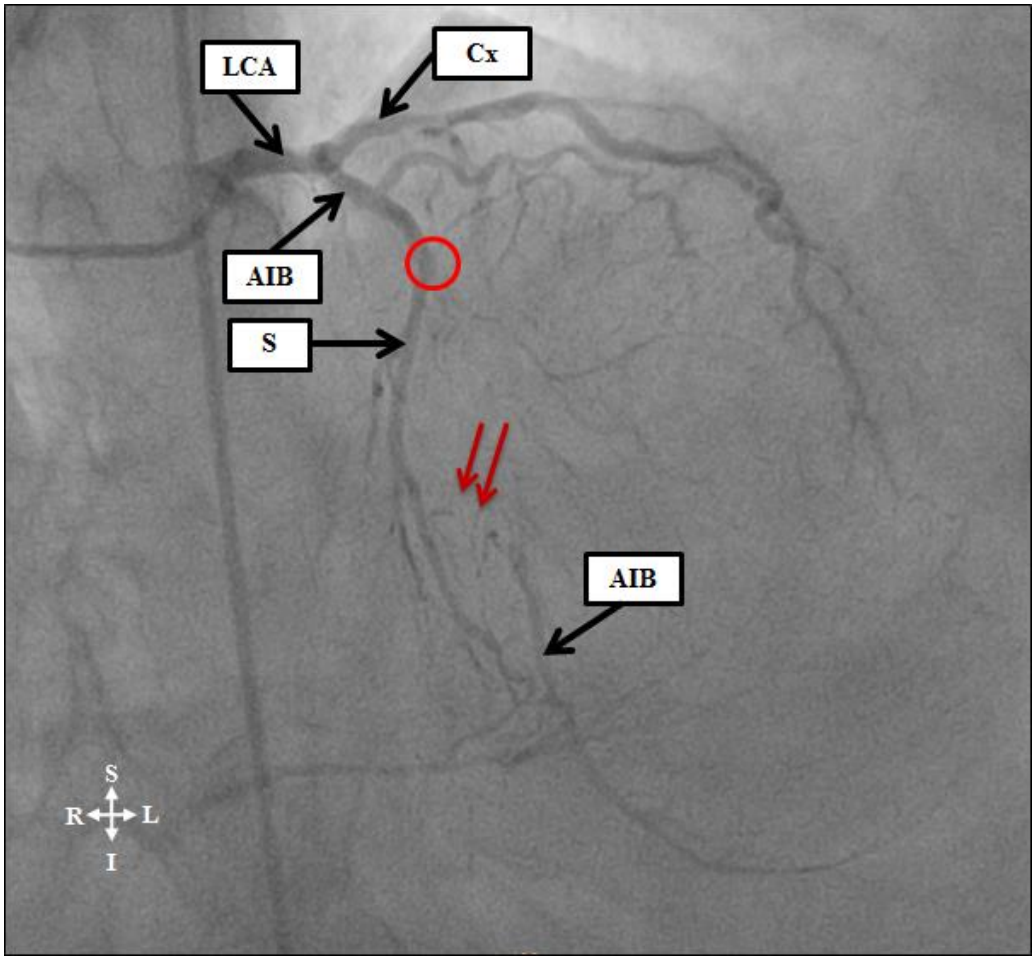

Plate 8: *Coronary angiogram in the RAO view (cranial angulation) showing the filling of the distal segment of the anterior interventricular branch obstructed at its mid- segment (red ring) by collateral vessels (red arrows) originating from the septal branch (segment 17) and terminating at the distal segment of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **S**=septal branch of anterior interventricular branch

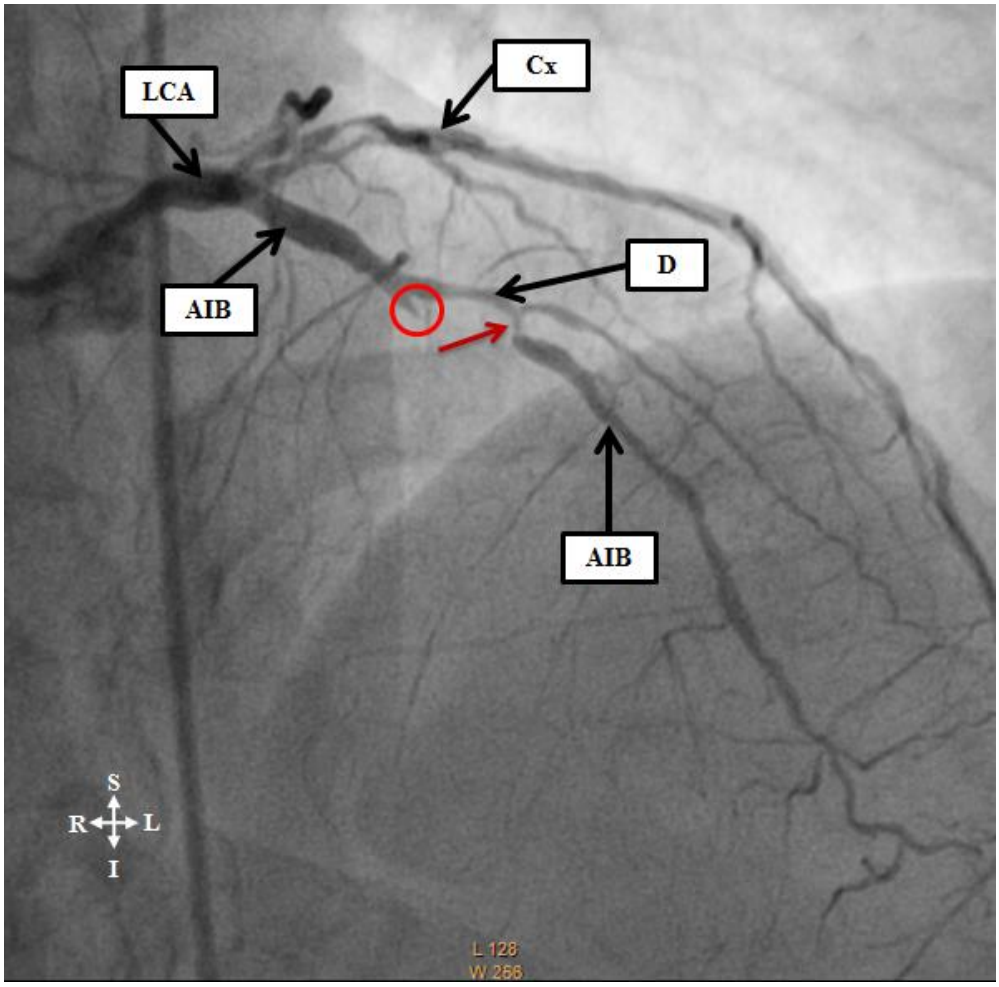

Plate 9: *Coronary angiogram in the RAO view (cranial angulation) showing the filling of the distal segment of the anterior interventricular branch obstructed at its mid- segment (red ring) by collateral vessel (red arrow) originating from the diagonal branch (segment 15) and terminating at the mid-segment of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **D**=diagonal branch of anterior interventricular branch

(iii) Segment 14

In the angiograms with total obstruction of the anterior interventricular branch, *segment 14* of the anterior interventricular branch was totally obstructed in two coronary angiograms. In both angiograms, coronary collaterals originated from *segment 20* of the circumflex and terminated in *segment 14* of the anterior interventricular branch (Plate 10).

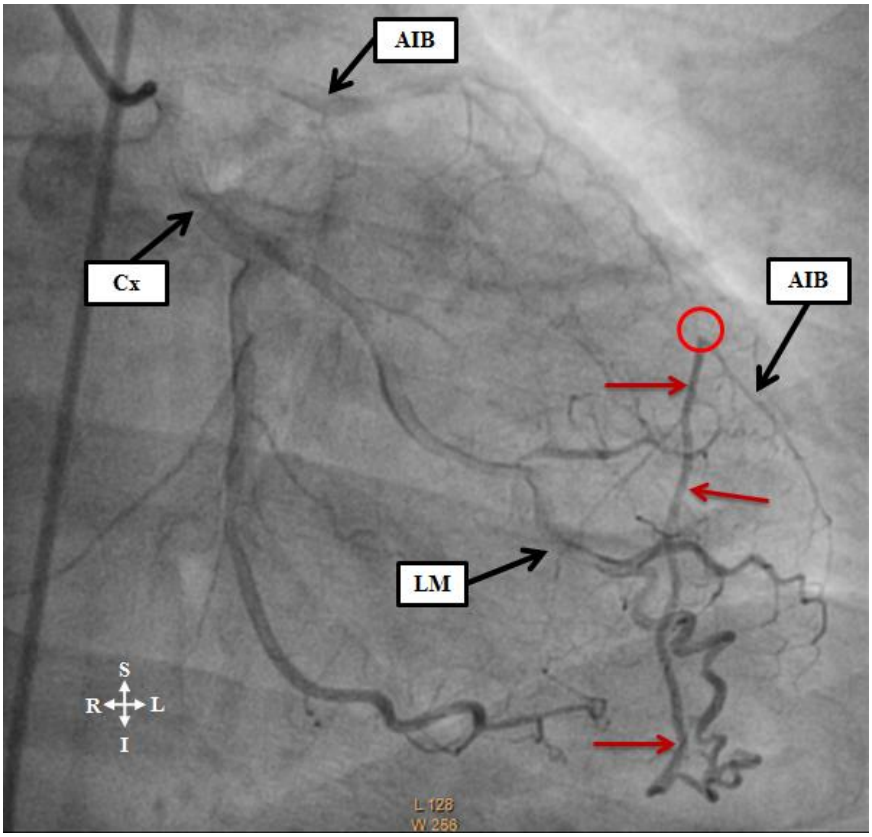

Plate 10: *Coronary angiogram in the RAO view (caudal angulation) showing the filling of the distal segment of an obstructed anterior interventricular branch (red ring) by collateral vessel (red arrows) originating from the left marginal branch (segment 20) of circumflex branch and terminating at the distal segment of the anterior interventricular branch*

Key: **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **LM**=left marginal branch of circumflex branch

(iv) Segment 15

In the angiograms with total obstruction of the anterior interventricular branch, *segment 15* of the anterior interventricular branch was totally obstructed in eight coronary angiograms. Six collateral pathways were recorded in five coronary angiograms with collaterals and collaterals were absent in two of the angiograms (Table 4; Plate 11).

***Table 4**: Coronary collateral pathways in the total obstruction of segment 15 of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	14	15	2
2	20	15	1
3	15	15	2
4	12	15	1
			6

(v) Segment 16

Segment 16 of the anterior interventricular branch was totally obstructed in three coronary angiograms. Three different collateral pathways were recorded in these angiograms (Table 5).

***Table 5**: Coronary collateral pathways in the total obstruction of segment 16 of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	20	16	1
2	13	16	1
3	16	16	1

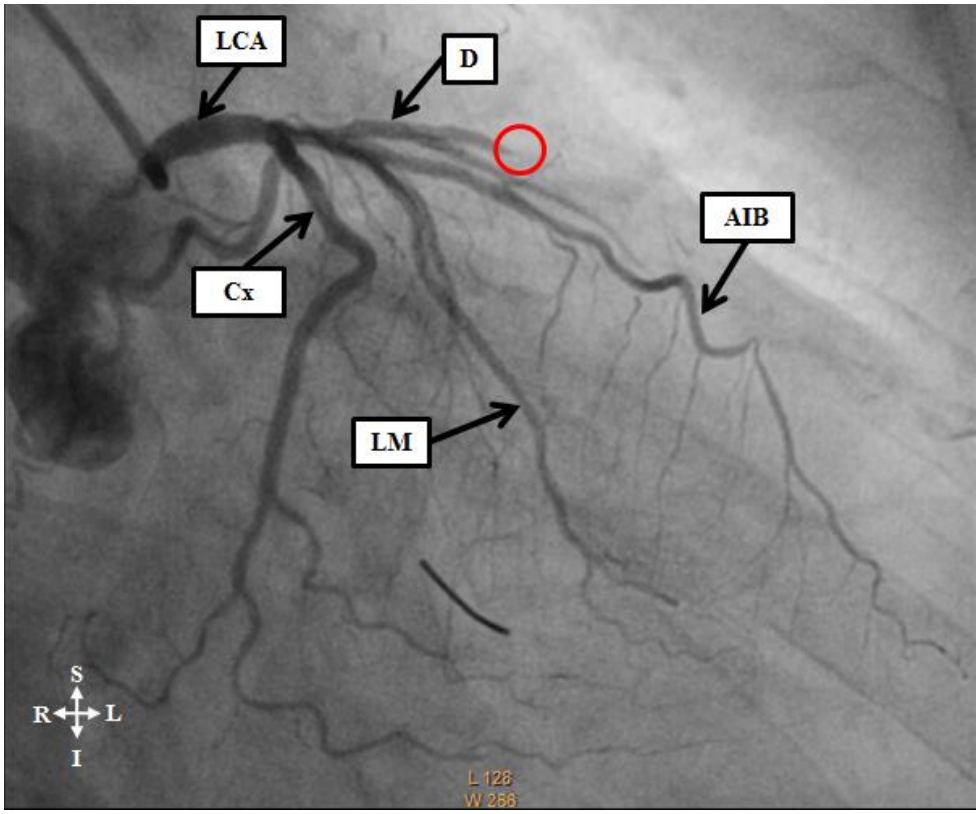

Plate 11: *Coronary angiogram in the RAO view (caudal angulation) showing obstruction of the diagonal branch (segment 15) of the anterior interventricular branch (red ring) without collateral vessel to the distal segment of the obstructed vessel*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **D**=diagonal branch of anterior interventricular branch, **LM**=left marginal branch of circumflex branch

4.4.2 THE CIRCUMFLEX BRANCH

The total obstruction of the circumflex branch (in any of its segments) was recorded in 87 of the coronary angiograms analyzed. In some of the angiograms with total obstruction of the circumflex branch, there were no coronary collaterals to the distal segment(s) of the circumflex branch, while some had more than one coronary collateral pathway.

Segment 18

In the angiograms with total obstruction of the circumflex branch, *segment 18* of the circumflex branch was totally obstructed in 30 coronary angiograms. Twenty-one collateral pathways were recorded in 15 of these coronary angiograms with collaterals to the circumflex branch (Table 6; Plates 12-13).

Table 6*: Coronary collateral pathways in the total obstruction of segment 18 of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	10	20	1
2	6	24	1
3	5	23	2
4	16	21	1
5	20	24	1
6	22	24	1
7	14	21	1
8	5	19a	2
9	18	18	3
10	16	19a	2
11	3	23	2
12	Right atrial branch	23	1
13	18	19	1
14	16	20	1
15	14	27	1
			21

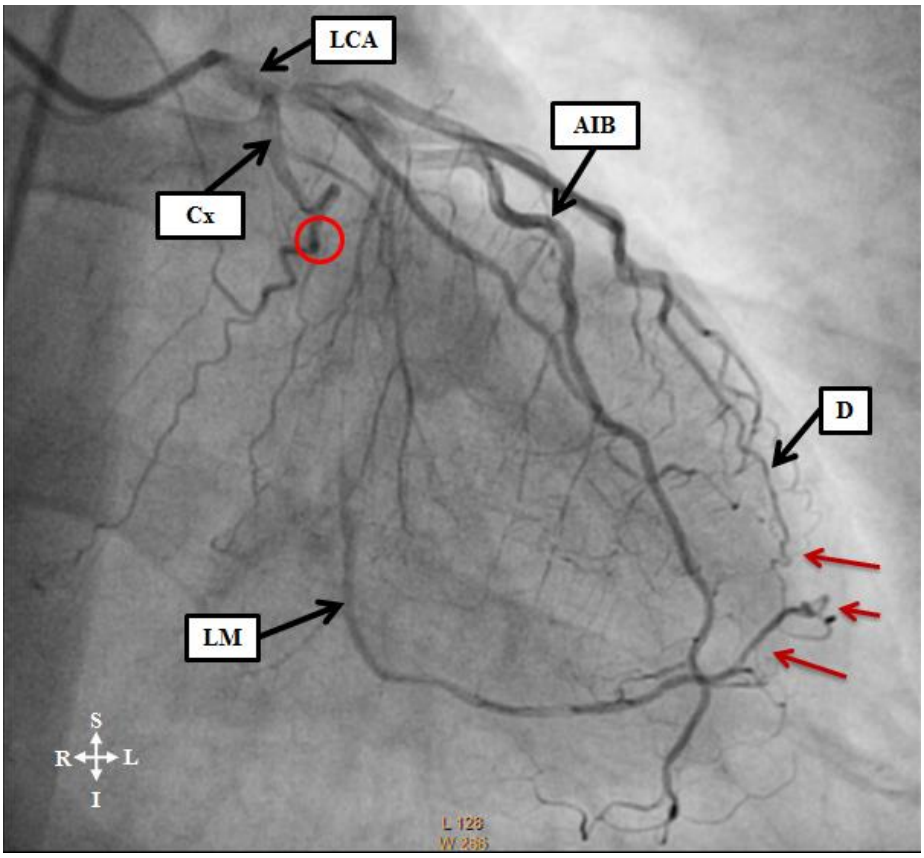

Plate 12: *Coronary angiogram in the RAO view (caudal angulation) showing obstruction of the circumflex branch (segment 18) (red ring) with the filling of the left marginal branch (segment 21) of the circumflex branch by collateral vessel (red arrows) originating from the diagonal branch (segment 16) of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **D**=diagonal branch of anterior interventricular branch, **LM**=left marginal branch of circumflex branch

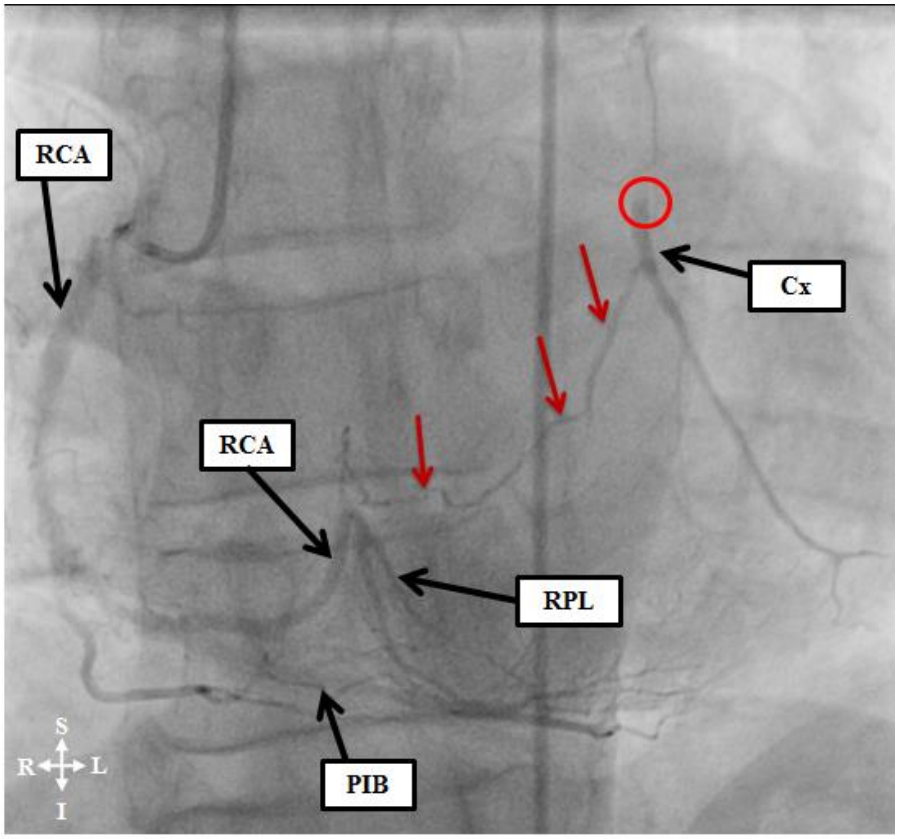

Plate 13: *Coronary angiogram in the LAO view (caudal angulation) showing obstruction of the circumflex branch (red ring) with the filling of the distal circumflex branch (segment 19a) by collateral vessel (red arrows) originating from the distal RCA (segment 5)*

Key: **RCA**=right coronary artery, **PIB**=posterior interventricular branch, **Cx**=circumflex branch, **RPL**=right postero-lateral branch

(i) Segment 19

In the angiograms with total obstruction of the circumflex branch, *segment 19* of the circumflex branch was totally obstructed in 23 coronary angiograms. Coronary collaterals were absent in two of these angiograms and 20 collateral pathways were recorded in the remaining 15 coronary angiograms with collaterals to the circumflex branch (Table 7; Plate 14).

***Table 7**: Coronary collateral pathways in the total obstruction of segment 19 of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	14	27	2
2	17	9	1
3	7	19a	1
4	15	23	1
5	19	5	1
6	13	27	1
7	17	27	1
8	20	21	1
9	20	19a	1
10	21	19a	1
11	19	19	1
12	5	23	1
13	18	19a	1
14	4	23	1
15	16	21	1
16	18	19	1
17	17	22	1
18	18	23	1
19	17	23	1
			20

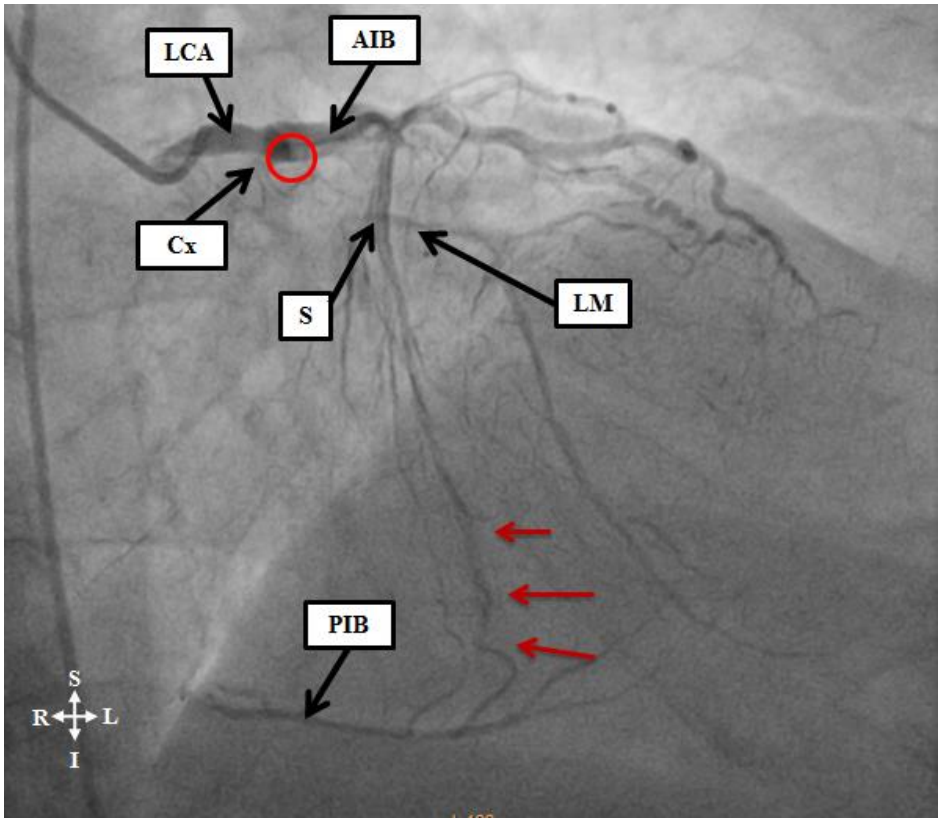

Plate 14: *Coronary angiogram in the RAO view (caudal angulation) showing proximal obstruction of the circumflex branch (red ring) with the filling of the* posterior interventricular branch *(segment 27) of the circumflex branch by collateral vessel (red arrows) originating from the septal branch (segment 17) of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **S**=septal branch of anterior interventricular branch, **LM**=left marginal branch of circumflex branch, **PIB**=posterior interventricular branch

(ii) Segment 19a

Segment 19a of the circumflex branch was totally obstructed in 11 coronary angiograms. Coronary collaterals were absent in two of these angiograms and 10 collateral pathways were recorded in the remaining nine coronary angiograms (Table 8; Plate 15).

***Table 8**: Coronary collateral pathways in the total obstruction of segment 19a of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	7	19a	1
2	5	19a	1
3	20	22	2
4	19a	23	2
5	19a	19a	1
6	21	23	1
7	17	27	1
8	21	19a	1
			10

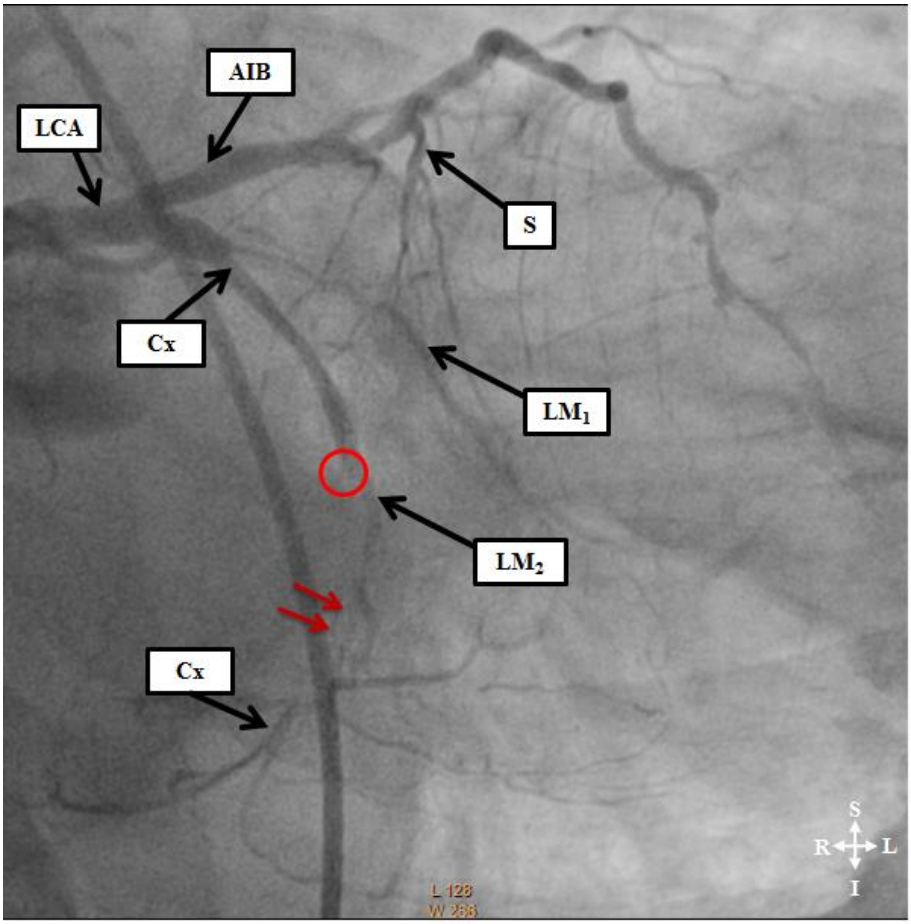

Plate 15: *Coronary angiogram in the RAO view (caudal angulation) showing obstruction of the circumflex branch (red ring) with the filling of the distal circumflex branch (segment 23) by collateral vessel (red arrows) originating from the second left marginal branch (segment 21) of the circumflex branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **Cx**=circumflex branch, **S**=septal branch of anterior interventricular branch, **LM_1**=first left marginal branch, **LM_2**=second left marginal branch

(iii) Segment 20

This segment of the circumflex branch was totally obstructed in 10 coronary angiograms. Seven collateral pathways were recorded in seven of these coronary angiograms with collaterals (Table 9).

***Table 9**: Coronary collateral pathways in the total obstruction of segment 20 of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	15	20	2
2	18	20	2
3	20	20	1
4	21	20	1
5	14	20	1
			7

(iv) Segment 21

The total obstruction of this segment was recorded in seven coronary angiograms. All the angiogram had a collateral pathway to the obstructed vessel (Table 10).

***Table 10**: Coronary collateral pathways in the total obstruction of segment 21 of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	20	21	3
2	22	21	1
3	21	21	1
4	19	21	1
5	15	21	1
			7

(v) Segment 23

This segment of the circumflex branch was totally obstructed in six coronary angiograms. Six collateral pathways were recorded in five of the angiogram that had collaterals vessels (Table 11).

***Table 11**: Coronary collateral pathways in the total obstruction of segment 23 of circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	5	23	1
2	19	23	1
3	19a	23	1
4	Right ventricular branch	27	1
5	19	27	1
6	17	27	1
			6

4.4.3 THE RIGHT CORONARY ARTERY

The total obstruction of the RCA (in any of its segments) was recorded in 166 of the coronary angiograms analyzed.

(i) Segment 1

Segment 1 of the RCA was totally obstructed in 69 coronary angiograms. A total of 96 collateral pathways were recorded in 53 of these coronary angiograms with coronary collaterals (Table 12; Plates 16-19).

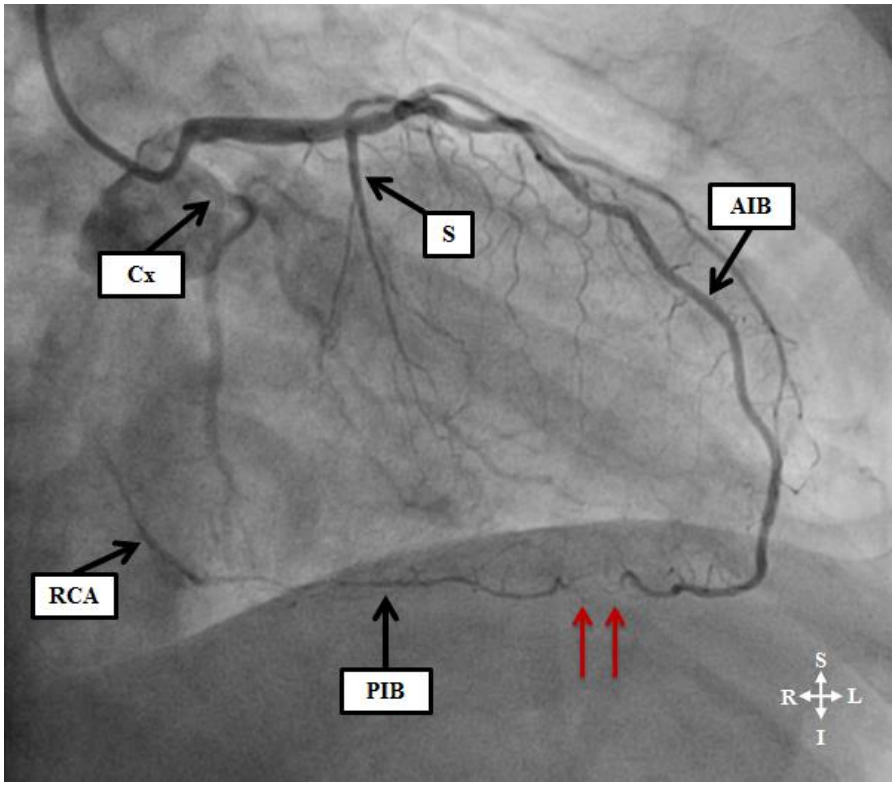

Plate 16: *Coronary angiogram in the RAO view (caudal angulation) showing filling of the* posterior interventricular branch *(segment 4) of the RCA by collateral vessel (red arrows) originating from the distal anterior interventricular branch (segment 14)*

Key: **LCA**=left coronary artery**, AIB**=anterior interventricular branch, **Cx**=circumflex branch, **S**=septal branch of anterior interventricular branch, **PIB**=posterior interventricular branch

***Table 12**: Coronary collateral pathways in the total obstruction of segment 1 of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	14	4	9
2	1	10	4
3	17	9	29
4	23	4	4
5	Conal branch	1	1
6	22	4	2
7	1	2	15
8	21	4	1
9	1	1	5
10	18	5	6
11	14	Right ventricular branch	1
12	SA node branch	Right ventricular branch	1
13	1	3	1
14	19a	4	3
15	19a	5	3
16	23	5	2
17	Conal branch	Right ventricular branch	1
18	19	5	1
19	19	4	2
20	14	3	1
21	23	3	1
22	Conal branch	10	1
23	18	4	1
24	1	5	1
			96

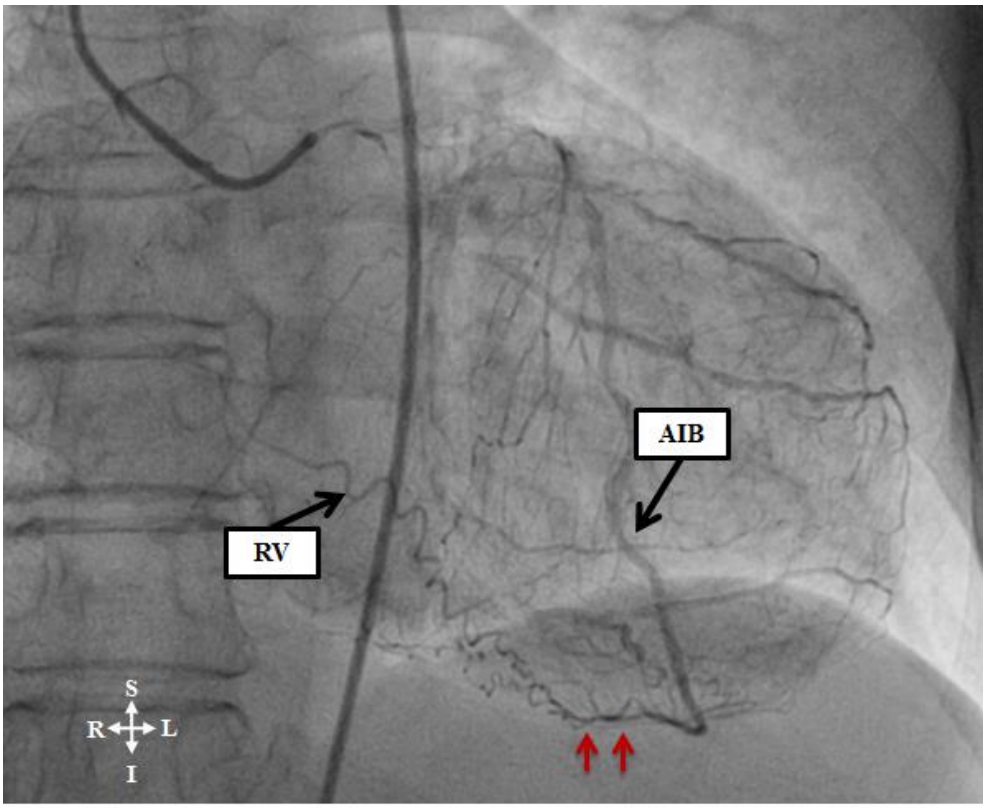

Plate 17: *Coronary angiogram in the RAO view (caudal angulation) showing filling of the RV branch of the RCA by collateral vessels (red arrows) originating from the distal anterior interventricular branch (segment 14)*

Key: **AIB**=anterior interventricular branch, **RV**=right ventricular branch

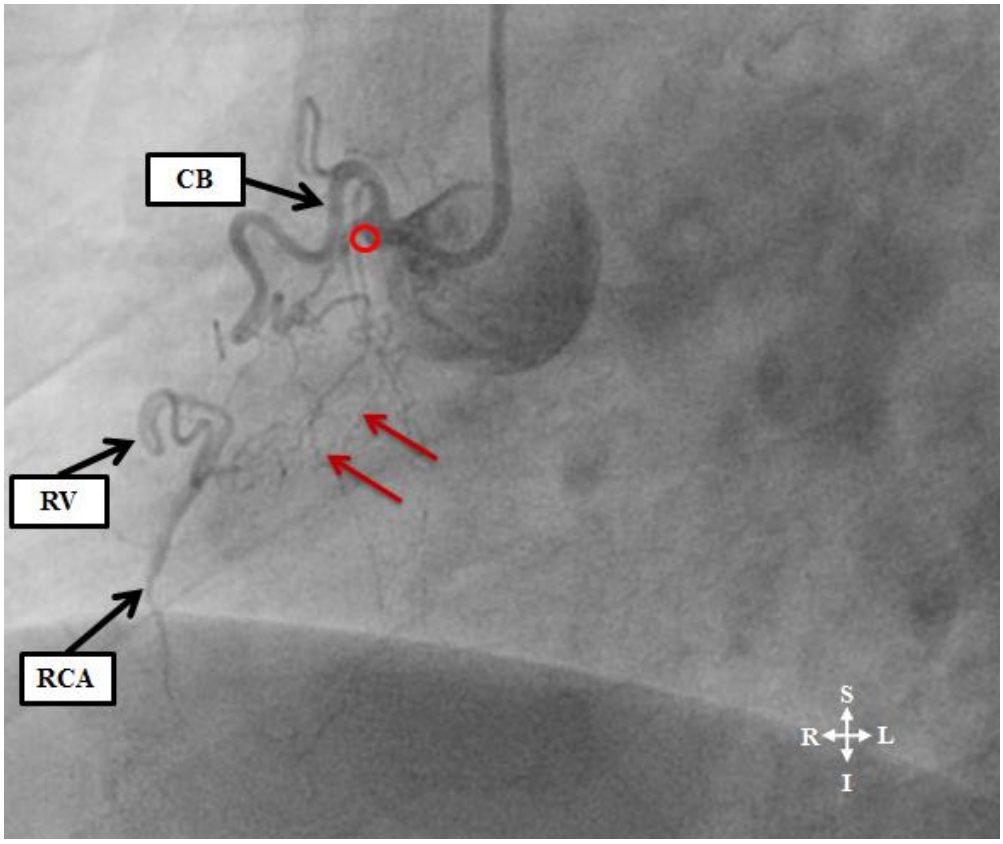

Plate 18: *Coronary angiogram in the LAO view (cranial angulation) showing filling of the RV branch of the RCA by collateral vessels (red arrows) originating from the CB of the RCA which is obstructed in its proximal segment (red ring)*

Key: **RCA**=right coronary artery**, CB**=conal branch, **RV**=right ventricular branch

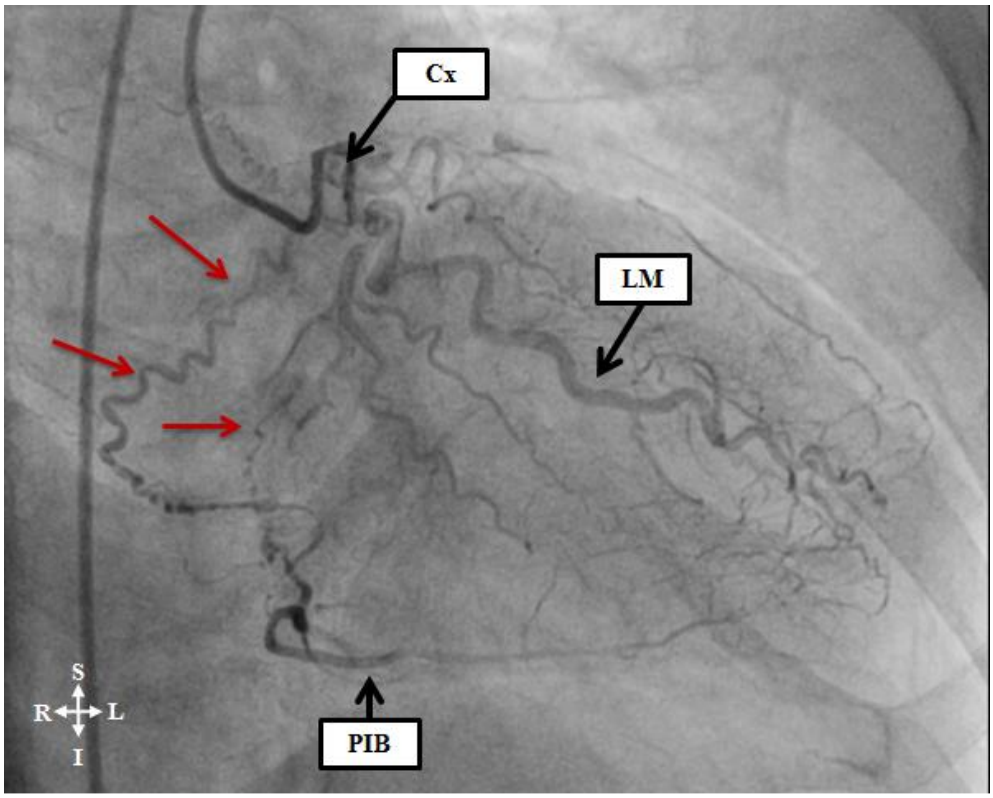

Plate 19: *Coronary angiogram in the RAO view (caudal angulation) showing filling of the* posterior interventricular branch *(segment 4) of the RCA by collateral vessels (red arrows) originating from segments 18 and 19a of the circumflex branch*

Key: **PIB**=posterior interventricular branch, **Cx**=circumflex branch, **LM**=left marginal branch

(ii) Segment 2

Segment 2 was totally obstructed in 65 coronary angiograms. A total of 76 collateral pathways were recorded in 55 of these coronary angiograms with coronary collaterals (Table 13; Plates 20-21).

***Table 13**: Coronary collateral pathways in the total obstruction of segment 2 of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	17	9	28
2	23	9	1
3	2	2	11
4	18	5	3
5	23	4	1
6	10	2	1
7	Right ventricular branch	4	2
8	1	4	1
9	14	4	8
10	23	5	2
11	19a	4	1
12	1	2	2
13	18	4	1
14	19a	5	1
15	21	6	1
16	21	7	1
17	19	5	3
18	2	3	2
19	13	4	1
20	18	3	2
21	19a	3	2
22	20	4	1

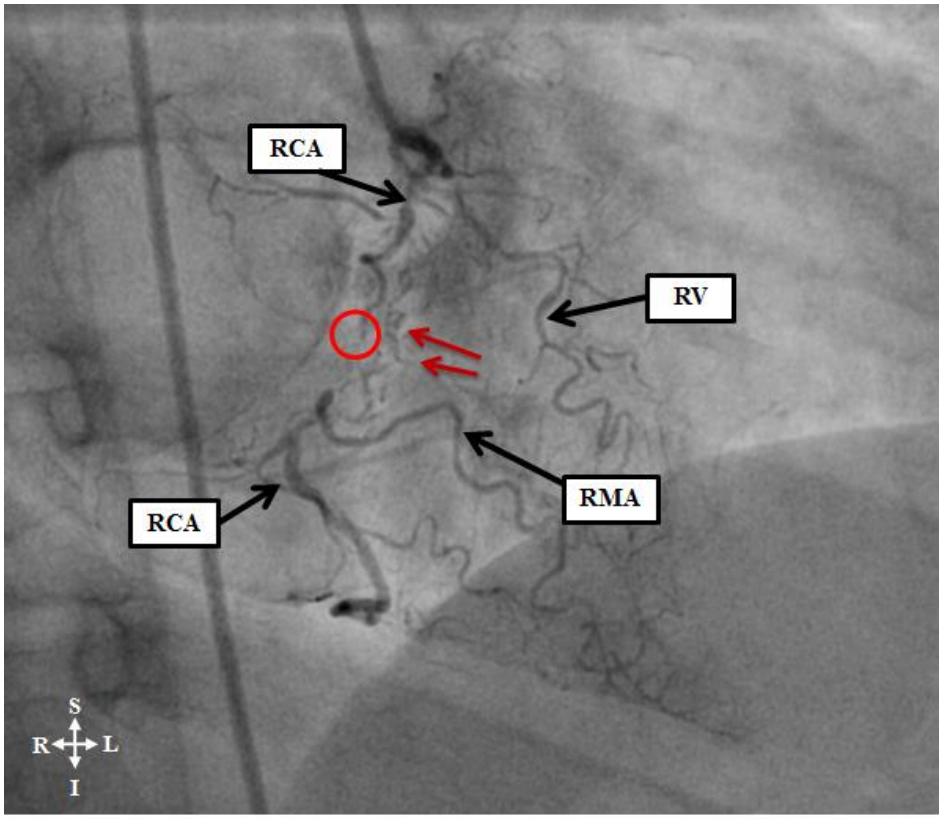

Plate 20: *Coronary angiogram in the RAO view (caudal angulation) showing obstruction of the RCA (red ring) in segment 2 with bridging collateral vessels (red arrows) originating from proximal to distal RCA regions*

Key: **RCA**=right coronary artery, **RV**=right ventricular, **RMA**= right marginal artery

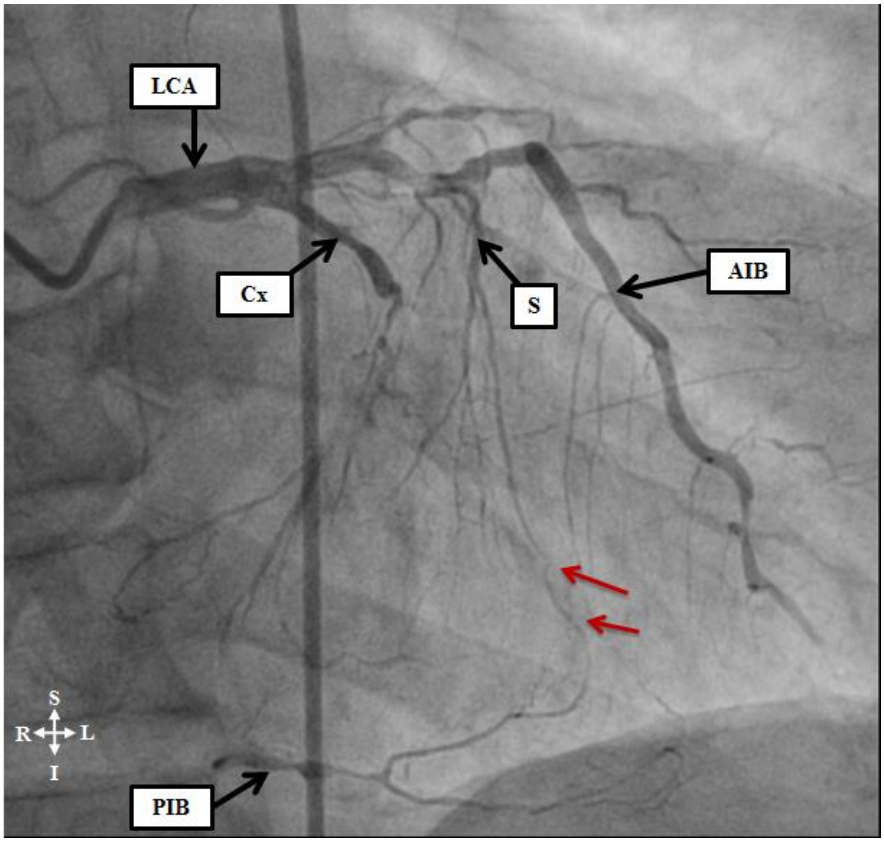

Plate 21: *Coronary angiogram in the RAO view showing the filling of the* posterior interventricular branch *(segment 4) of an obstructed RCA (in segment 2) with collateral vessels (red arrows) originating from the septal branch (segment 17) of the anterior interventricular branch*

Key: **LCA**=left coronary artery, **AIB**=anterior interventricular branch, **S**=septal branch **PIB**=posterior interventricular branch, **Cx**=circumflex branch

(iii) Segment 3

Segment 3 was totally obstructed in 15 coronary angiograms. A total of 19 collateral pathways were recorded in 13 of these coronary angiograms with coronary collaterals (Table 14).

***Table 14**: Coronary collateral pathways in the total obstruction of segment 3 of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	17	9	9
2	23	5	1
3	10	4	1
4	24	4	1
5	23	6	1
6	23	4	1
7	14	4	1
8	21	4	1
9	18	5	2
10	3	3	3
11	19	5	2
			23

(iv) Segment 4

Segment 4 was totally obstructed in 10 coronary angiograms. A total of nine collateral pathways were recorded in eight of these coronary angiograms (Table 15).

***Table 15**: Coronary collateral pathways in the total obstruction of segment 4 of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	18	19a	1
2	19	4	1
3	17	9	4
4	14	4	2
5	4	4	1

(v) Segment 5

Segment 5 was totally obstructed in two coronary angiograms and each had a collateral pathway (Table 16).

***Table 16**: Coronary collateral pathways in the total obstruction of segment 5 of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	6	7	1
2	19	5	1

4.5 SUMMARY OF THE ANATOMIC PATHWAYS OF THE CORONARY COLLATERALS

In order to determine the number of the different coronary collateral pathways identified in the obstruction of the segments of the main coronary arteries, the collateral pathways that occurred more than once in the obstruction of the different segments of the same coronary artery were counted once. Therefore, in the obstruction of the different segments of the main coronary arteries, a total of *115 different collateral pathways* were observed as follows: ***anterior interventricular branch - n=32*** (Table 17), ***circumflex branch – n=46*** (Table 18) and ***RCA- n=37*** (Table 19).

Table 17*: Summary of coronary collateral pathways in the total obstruction of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	23	14	1
2	9	17	8
3	20	14	6
4	28	14	1
5	21	13	1
6	17	13	3
7	Right ventricular branch	13	3
8	12	13	3
9	4	12	1
10	9	12	2
11	10	14	1
12	Right ventricular branch	14	4
13	9	14	2
14	10	13	1
15	28	13	1

***Table 17 continued**: Summary of coronary collateral pathways in the total obstruction of the anterior interventricular branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
16	15	13	2
17	4	14	3
18	Right conal branch	12	2
19	17	17	2
20	13	13	4
21	15	16	1
22	9	13	2
23	14	15	2
24	20	15	1
25	15	15	2
26	12	15	1
27	20	16	1
28	13	16	1
29	16	16	1
30	21	4	1
31	17	12	1
32	27	14	1

***Table 18**: Summary of coronary collateral pathways in the total obstruction of the circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	10	20	1
2	6	24	1
3	5	23	4
4	16	21	2
5	20	24	1
6	22	24	1
7	14	21	1
8	5	19a	2
9	18	18	3
10	16	19a	2
11	3	23	2
12	Right atrial branch	23	1
13	18	19	2
14	16	20	1
15	7	19a	2
16	20	22	2
17	19a	23	3
18	19a	19a	1
19	21	23	1
20	17	27	3
21	15	20	2
22	18	20	2
23	20	20	2

***Table 18 continued**: Summary of coronary collateral pathways in the total obstruction of the circumflex branch*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
24	21	20	1
25	20	21	4
26	22	21	1
27	21	21	1
28	19	21	1
29	15	21	1
30	19	23	1
31	Right ventricular branch	27	1
32	19	27	1
33	14	27	3
34	17	9	2
35	15	23	1
36	19	5	1
37	13	27	1
38	20	19a	1
39	21	19a	2
40	19	19	1
41	18	19a	1
42	4	23	1
43	17	22	1
44	18	23	1
45	17	23	1
46	14	20	1

***Table 19**: Summary of coronary collateral pathways in the total obstruction of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
1	14	4	20
2	1	10	4
3	17	9	70
4	23	4	6
5	Conal branch	1	1
6	22	4	2
7	1	2	17
8	21	4	2
9	1	1	5
10	18	5	11
11	14	Right ventricular branch	1
12	SA node branch	Right ventricular branch	1
13	1	3	1
14	19a	4	4
15	19a	5	4
16	23	5	5
17	Conal branch	Right ventricular branch	1
18	19	5	7
19	19	4	3
20	14	3	1
21	23	3	1
22	Conal branch	10	1
23	18	4	2

***Table 19 continued**: Summary of coronary collateral pathways in the total obstruction of the RCA*

Pathway no	Origin of collateral vessel (Coronary segment)	Termination of collateral vessel (Coronary segment)	Frequency
24	10	4	1
25	24	4	1
26	23	6	1
27	3	3	3
28	18	19a	1
29	6	7	1
30	23	9	1
31	2	2	11
32	10	2	1
33	Right ventricular branch	4	2
34	1	4	1
35	21	6	1
36	21	7	1
37	2	3	2

In anterior interventricular branch obstructions, coronary collateral vessels originated from the anterior interventricular branch, circumflex branch, RCA and median branch and/or their branches in 37.5% ($^{12}/_{32}$), 21.9% ($^{7}/_{32}$), 34.4% ($^{11}/_{32}$) and 6.2% ($^{2}/_{32}$), respectively. In circumflex branch obstructions, collateral vessels were from the anterior interventricular branch, circumflex branch and RCA and/or their branches in 30.4% ($^{14}/_{46}$), 50% ($^{23}/_{46}$) and 19.6% ($^{9}/_{46}$), respectively. The collateral vessels in the RCA obstructions were from the anterior interventricular branch, circumflex branch and RCA

and/or their branches in 10.8% ($^{4}/_{37}$), 45.9% ($^{17}/_{37}$) and 43.2% ($^{16}/_{37}$), respectively (Table 20).

***Table 20**: Vessel of origin of the coronary collaterals in the obstruction of the main coronary arteries*

Obstructed coronary artery	**Vessel of origin of collateral arteries (%)**			
	Anterior interventricular branch	**Circumflex branch**	**RCA**	**Median branch**
Anterior interventricular branch	37.5	21.9	34.4	6.2
Circumflex branch	30.4	50	19.6	-
RCA	10.8	45.9	43.2	-

4.6 THE GRADES OF CORONARY COLLATERALS IN THE OBSTRUCTIONS OF THE CORONARY ARTERIES

The grades of the coronary collateral pathways (Page 71) documented in the obstruction of the main coronary arteries in the analyzed coronary angiograms were as follows (Figure 42; Plates 22-25):

a) Anterior interventricular branch - Absent, poor, good and excellent collaterals were 30.3% ($^{23}/_{76}$), 13.2% ($^{10}/_{76}$), 32.9% ($^{25}/_{76}$) and 23.7% ($^{18}/_{76}$), respectively.

b) Circumflex branch- Absent, poor, good and excellent collaterals were 33.3% ($^{29}/_{87}$), 19.5% ($^{17}/_{87}$), 29.9% ($^{26}/_{87}$) and 17.2% ($^{15}/_{87}$), respectively.

c) RCA- Absent, poor, good and excellent collaterals were 19.3% ($^{32}_{166}$), 10.8% ($^{18}/_{166}$), 39.2% ($^{65}/_{166}$) and 30.7% ($^{51}/_{166}$), respectively.

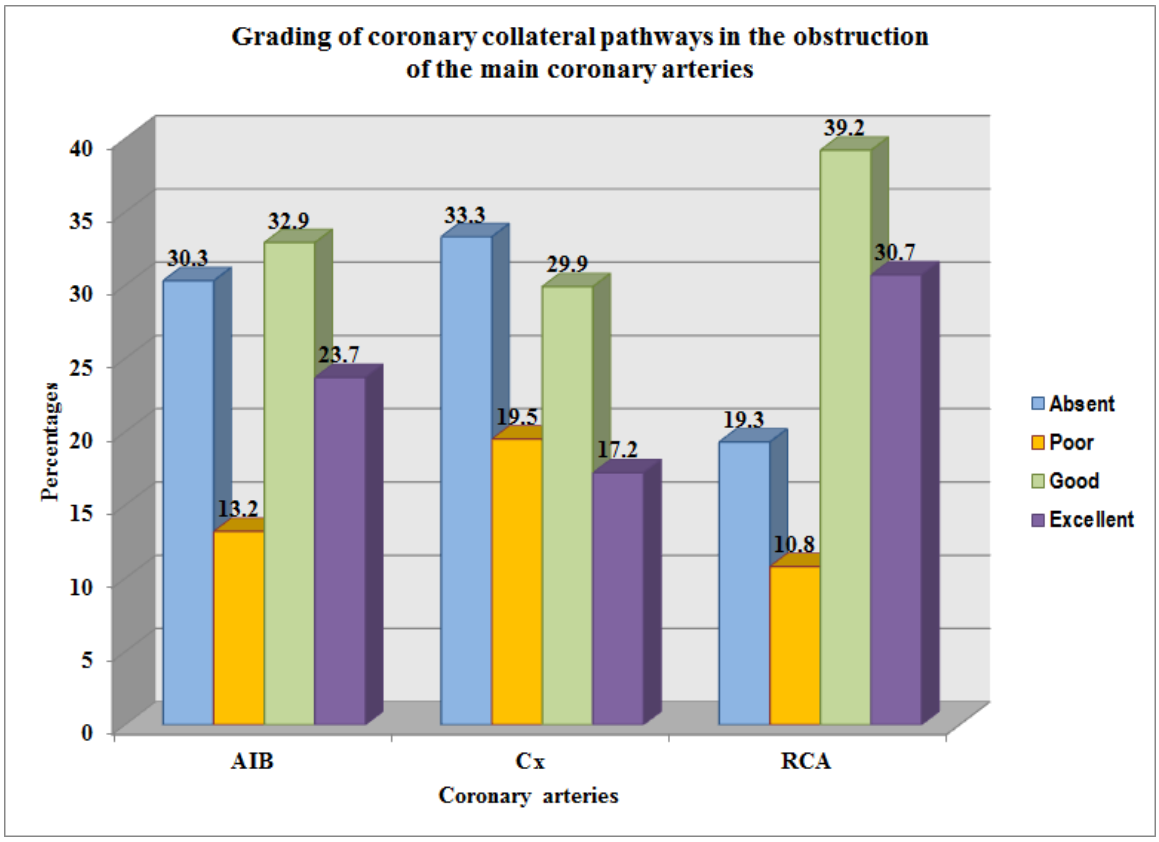

***Figure 42**: Grading of coronary collateral pathways in the obstruction of the main coronary arteries*

Key: **RCA** = right coronary artery, **Cx**= circumflex branch, **AIB**= anterior interventricular branch

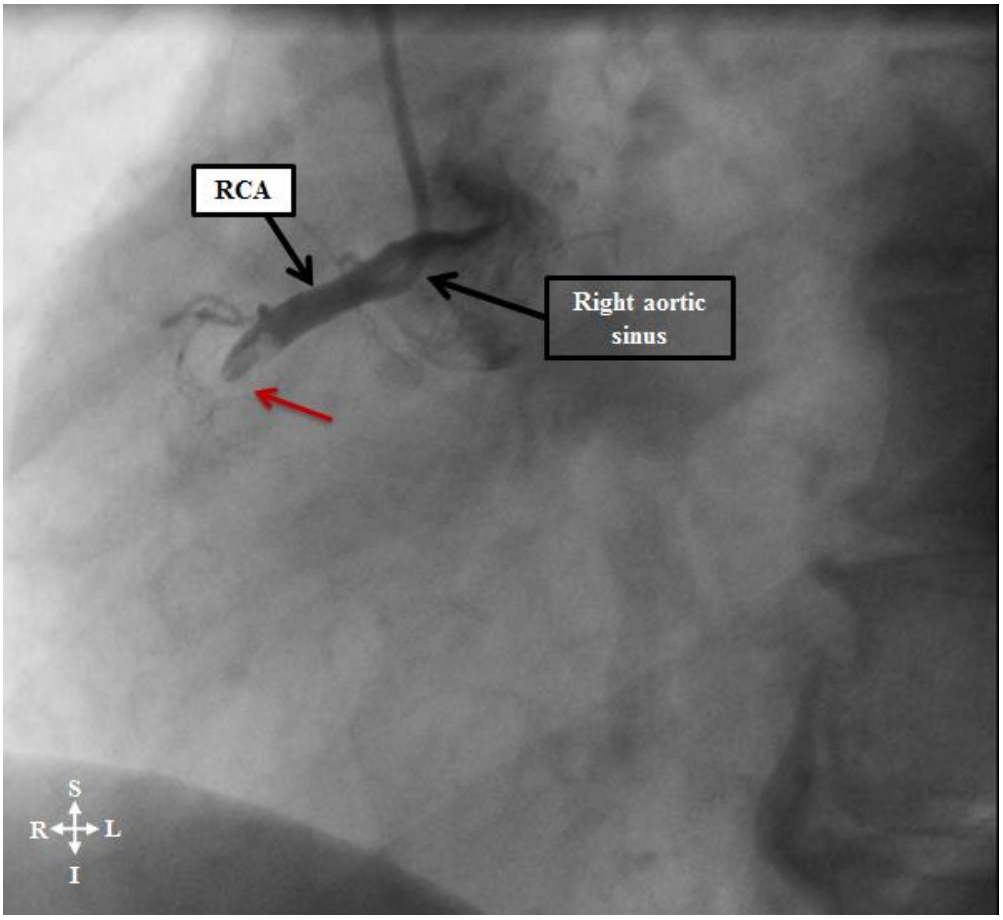

Plate 22: *Coronary angiogram in the LAO view showing total obstruction of the RCA (red arrows) without collateral vessels (**grade 0; absent**) to its distal segments*

Key: **RCA**= right coronary artery

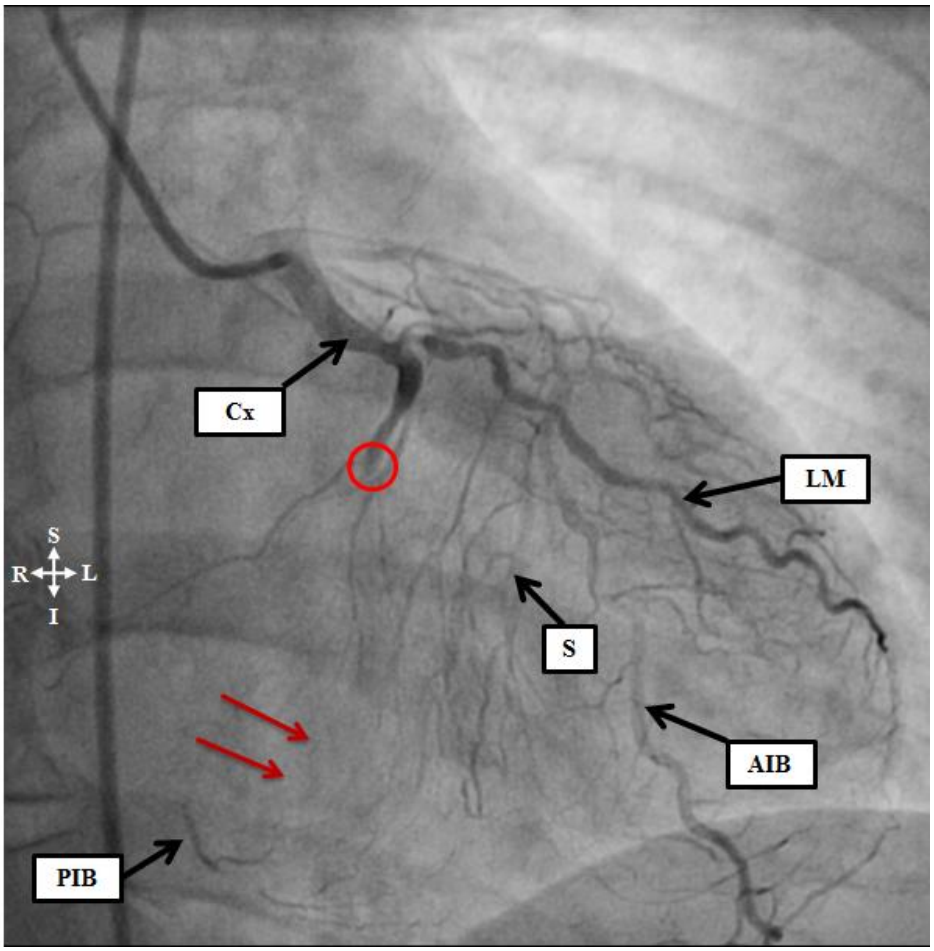

Plate 23: *Coronary angiogram in the RAO view showing the filling of the posterior interventricular branch (segment 27) of an obstructed (red ring) circumflex branch (in segment 19) with invisible collaterals (**grade 1; poor**; red arrows) originating from the septal branch (segment 17) of the anterior interventricular branch*

Key: **AIB**=anterior interventricular branch, **S**=septal branch **PIB**=posterior interventricular branch, **Cx**=circumflex branch, **LM**= left marginal

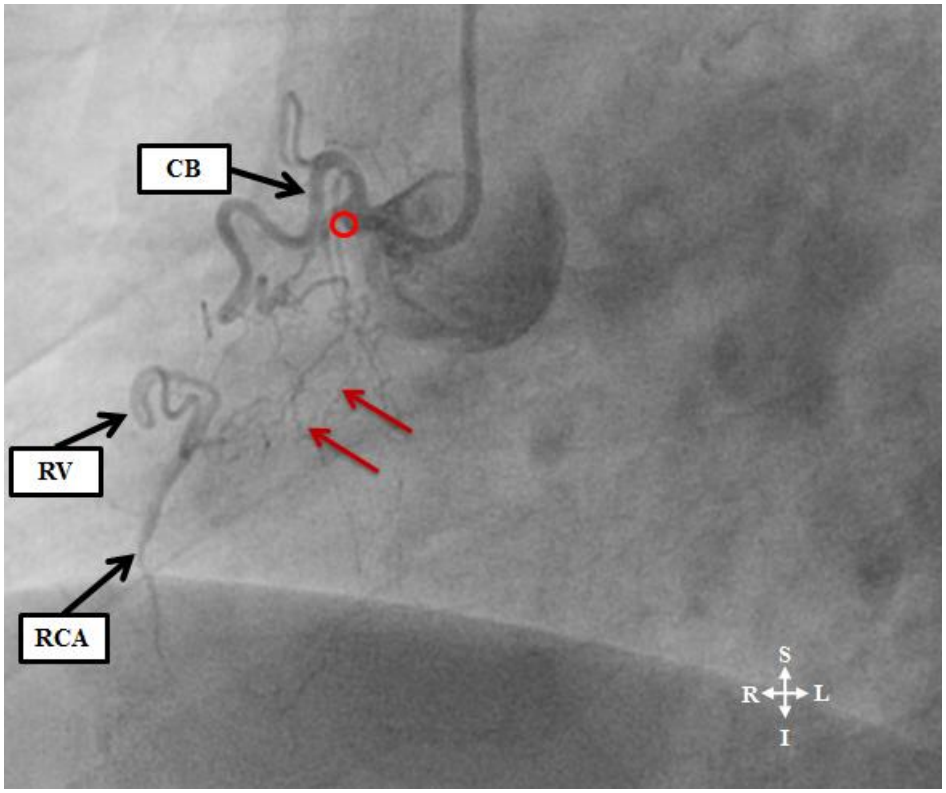

Plate 24: *Coronary angiogram in the LAO view (cranial angulation) showing filling of the RV branch of the RCA by* ***grade 2 (good)*** *collateral vessels (red arrows) originating from the CB of an obstructed RCA (red ring)*

Key: **RCA**=right coronary artery**, CB**=conal branch, **RV**=right ventricular branch

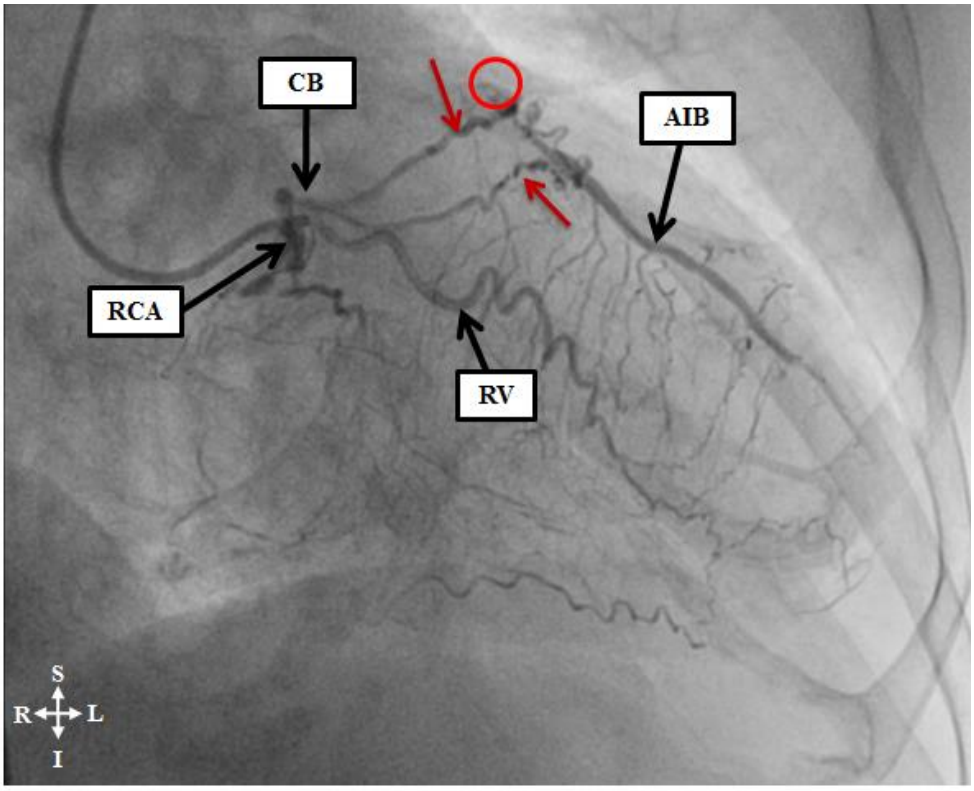

***Plate 25**: Coronary angiogram in the RAO view showing the filling of the anterior interventricular branch obstructed at its proximal segment (red ring) by **grade 3 (excellent)** collateral vessels (red arrows) originating from the CB and terminating at segment 12 of the anterior interventricular branch*

Key: **RCA**=right coronary artery, **AIB**=anterior interventricular branch, **CB**=conal branch, **RV**=right ventricular branch

4.6.1 GRADES OF CORONARY COLLATERALS IN RELATION TO AGE

In assessing the influence of age on the development the collateral pathways, the patients were divided into two age groups viz. ≤ 60 years and > 60 years. This division was based on the mean age (59 years) of the patients in the coronary angiograms selected for analysis. The grades of the collateral pathways (Page 71) to the obstructed arteries were documented and compared with respect to the different age groups.

a) ANTERIOR INTERVENTRICULAR BRANCH

The mean age of the patients was 57.2 ± 11.6 years (range 31 – 87 years). The grades of the collateral pathways in the obstruction of the anterior interventricular branch in the ≤ 60 years age group were recorded as 33.3% ($^{13}/_{39}$), 17.9% ($^{7}/_{39}$), 30.8% ($^{12}/_{39}$) and 17.9% ($^{7}/_{39}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the > 60 years age group were recorded as 22.6% ($^{7}/_{31}$), 9.7% ($^{3}/_{31}$), 35.5% ($^{11}/_{31}$) and 32.3% ($^{10}/_{31}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals in the different age groups in anterior interventricular branch obstructions (p = 0.38) (Table 21).

Table 21: *Grading of the coronary collateral pathways in the different age groups in the obstructions of the main coronary arteries.*

Coronary artery	Age Group	Grades of collateral vessel (%)				*P*-value
		Absent	Poor	Good	Excellent	
Anterior interventricular branch	≤ 60 years	33.3	17.9	30.8	17.9	0.38
	> 60 years	22.6	9.7	35.5	32.3	
Circumflex branch	≤ 60 years	22.5	22.5	30	25	0.1
	> 60 years	47.4	18.4	23.7	10.5	
RCA	≤ 60 years	18	12.4	30.3	39.3	0.06
	> 60 years	22.1	8.8	47.1	22.1	

b) CIRCUMFLEX BRANCH

The mean age of the patients was 60 ± 9.8 years (range 43 – 86 years). In the ≤ 60 years age group, the collateral pathways were graded as follows: absent- 22.5% ($^{9}/_{40}$), poor- 22.5% ($^{9}/_{40}$); good- 30% ($^{12}/_{40}$) and excellent- 25% ($^{10}/_{40}$). The grades of the collateral pathways in the obstruction of the circumflex branch in the > 60 years age group *were* recorded as 47.4% ($^{18}/_{38}$), 18.4% ($^{7}/_{38}$), 23.7% ($^{9}/_{38}$) and 10.5% ($^{4}/_{38}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals in the different age groups in circumflex branch obstructions ($p = 0.1$) (Table 21).

c) RIGHT CORONARY ARTERY

The mean age of the patients was 58.6 ± 10.3 years (range 29 – 93 years). The grades of the collateral pathways in the obstruction of the RCA in the ≤ 60 years *age group* were recorded as 18% ($^{16}/_{89}$), 12.4% ($^{11}/_{89}$), 30.3% ($^{27}/_{89}$) and 39.3% ($^{35}/_{89}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the > 60 years age group were recorded as 22.1% ($^{15}/_{68}$), 8.8% ($^{6}/_{68}$), 47.1% ($^{32}/_{68}$) and 22.1% ($^{15}/_{52}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals in the different age groups in RCA obstructions ($p = 0.06$) (Table 21).

4.6.2 GRADES OF CORONARY COLLATERALS IN RELATION TO SEX

a) ANTERIOR INTERVENTRICULAR BRANCH

The grades of the collateral pathways in the obstruction of the anterior interventricular branch in females were recorded as 31.3% ($^{5}/_{16}$), 6.3% ($^{1}/_{16}$), 43.8% ($^{7}/_{16}$) and 18.8% ($^{3}/_{16}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the anterior interventricular branch in males were recorded as 30% ($^{18}/_{60}$), 15% ($^{9}/_{60}$), 30% ($^{18}/_{60}$) and 25% ($^{15}/_{60}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals between females and males in anterior interventricular branch obstructions (p = 0.64) (Table 22).

***Table 22**: Grading of the coronary collateral pathways in females and males in the obstruction of the main coronary arteries.*

Coronary artery	Sex	Grades of collateral vessel (%)				*P*-value
		Absent	Poor	Good	Excellent	
AIB	Female	31.3	6.3	43.8	18.8	0.64
	Male	30	15	30	25	
Circumflex branch	Female	40	20	36	4	0.21
	Male	30.6	19.4	27.4	22.6	
RCA	Female	22.6	12.9	48.4	16.1	0.28
	Male	18.5	10.4	37	34.1	

b) CIRCUMFLEX BRANCH

The grades of the collateral pathways in the obstruction of the circumflex branch in females were recorded as 40% ($^{10}/_{25}$), 20% ($^{5}/_{25}$), 36% ($^{9}/_{25}$) and 4% ($^{1}/_{25}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the circumflex branch in males were recorded as 30.6% ($^{19}/_{62}$), 19.4% ($^{12}/_{62}$), 27.4% ($^{17}/_{62}$) and 22.6% ($^{14}/_{62}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals between females and males in circumflex branch obstructions ($p = 0.21$) (Table 22).

c) RIGHT CORONARY ARTERY

The grades of the collateral pathways in females in the obstruction of the RCA were recorded as 22.6% ($^{7}/_{31}$), 12.9% ($^{4}/_{31}$), 48.4% ($^{15}/_{31}$) and 16.1% ($^{5}/_{31}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in males in the obstruction of the RCA were recorded as 18.5% ($^{25}/_{135}$), 10.4% ($^{14}/_{135}$), 37% ($^{50}/_{135}$) and 34.1% ($^{46}/_{135}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals between females and males in RCA obstructions ($p = 0.28$) (Table 22). Therefore, there was no association between the patients' sex and the grading of coronary collateral vessel in RCA obstructions.

4.6.3 GRADES OF CORONARY COLLATERALS IN RELATION TO ATHEROSCLEROTIC LESION LOCATION IN THE ANALYZED ANGIOGRAMS

The main coronary arteries were divided into the proximal, middle and distal regions (Page 68). The grades of the collateral pathways (Page 71) to the obstructed arteries were documented with respect to the region of the artery in which the obstructions were located.

a) ANTERIOR INTERVENTRICULAR BRANCH

The grades of the collateral pathways in the obstruction of the *proximal region of the anterior interventricular branch* (segments 12, 15 and 15a) were recorded as 27.1% ($^{13}/_{48}$), 10.4% ($^{5}/_{48}$), 37.5% ($^{18}/_{48}$) and 25% ($^{12}/_{48}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the *middle region of the anterior interventricular branch* (segments 13, 16, 16a and 29) were recorded as 38.5% ($^{10}/_{26}$), 15.4% ($^{4}/_{26}$), 26.9% ($^{7}/_{26}$) and 19.2% ($^{5}/_{26}$) for absent, poor, good and excellent collaterals, respectively. The *distal region of the anterior interventricular branch* (segment 14) was obstructed in only two angiograms and the grades of the collateral pathways were recorded as poor and excellent each. There were no significant differences in the prevalence of the grades of coronary collaterals in the different regions in anterior interventricular branch obstructions ($p = 0.44$) (Table 23).

b) CIRCUMFLEX BRANCH

The grades of the collateral pathways in the obstruction of the *proximal region of the circumflex branch* (segments 18 and 20) were recorded as 45% ($^{18}/_{40}$), 15% ($^{6}/_{40}$), 25% ($^{10}/_{40}$) and 15% ($^{6}/_{40}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the - *middle region of the circumflex branch* (segments 19 and 21) were recorded as 26.7% ($^{8}/_{30}$), 26.7% ($^{8}/_{30}$), 33.3% ($^{10}/_{30}$) and 13.3% ($^{4}/_{30}$) for absent, poor, good and excellent collaterals, respectively. Sixteen collateral pathways were recorded in the obstruction of the *distal region of the circumflex branch* (segments 19a, 22, 23, 24, 25 and 26). The grades of these collateral pathways was recorded as follows: absent - 17.6% ($^{3}/_{17}$), poor - 17.6% ($^{3}/_{17}$), good - 35.3% ($^{6}/_{17}$) and excellent - 29.4% ($^{5}/_{17}$). There were no significant differences in the prevalence of the grades of coronary collaterals in the different regions in circumflex branch obstructions ($p = 0.32$) (Table 23).

c) RIGHT CORONARY ARTERY

The grades of the collateral pathways in the obstruction of the *proximal region of the RCA* (Segment 1) were recorded as 21.7% ($^{15}/_{69}$), 5.8% ($^{4}/_{69}$), 29% ($^{20}/_{69}$) and 43.5% ($^{20}/_{69}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the - *middle region of the RCA* (Segments 2 and 10) were recorded as 15.4% ($^{10}/_{65}$), 16.9% ($^{11}/_{65}$), 43.1% ($^{28}/_{65}$) and 24.6% ($^{16}/_{65}$) for absent, poor, good and excellent collaterals, respectively. In the obstruction of the *distal region of the RCA* (Segments 3, 4 and 5), the collateral pathways were graded as follows: absent- 21.9% ($^{7}/_{32}$), poor- 9.4% ($^{3}/_{32}$), good- 53.1% ($^{17}/_{32}$) and excellent- 15.6% ($^{5}/_{32}$).

There were significant differences in the prevalence of the grades of coronary collaterals in the different regions in RCA obstructions (p = 0.02) (Table 23). Therefore, there was an association between the location of obstructive atherosclerotic lesion and the grading of coronary collateral vessel in RCA obstructions.

***Table 23**: Grading of the coronary collateral pathways in the obstruction of the proximal, middle and distal regions of the main coronary arteries.*

Coronary artery	Region	Grading of collateral vessel (%)				*P*-value
		Absent	Poor	Good	Excellent	
AIB	Proximal	27.1	10.4	37.5	25	0.44
	Middle	38.5	15.4	26.9	19.2	
	Distal	-	50	-	50	
Cx	Proximal	45	15	25	15	0.32
	Middle	26.7	26.7	33.3	13.3	
	Distal	17.6	17.6	35.3	29.4	
RCA	Proximal	21.7	5.8	29	43.5	0.02
	Middle	15.4	16.9	43.1	24.6	
	Distal	21.9	9.4	53.1	15.6	

4.6.4 GRADES OF CORONARY COLLATERALS IN RELATION TO CORONARY ARTERIAL DOMINANCE

The effect of coronary arterial dominance on the grades of coronary collateral pathways was examined by documenting the prevalence of the coronary collateral grades in the different dominant patterns.

a) ANTERIOR INTERVENTRICULAR BRANCH

The grades of the collateral pathways in the co-dominant pattern were recorded as 33.3% and 66.7% for absent and poor collaterals, respectively. The grades of the collateral pathways in the left dominant pattern were recoded as 27.3% ($^{3}/_{11}$), 18.2% ($^{2}/_{11}$), 45.5% ($^{5}/_{11}$) and 9.4% ($^{1}/_{11}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the right dominant pattern were recorded as 30.6% ($^{19}/_{62}$), 9.7% ($^{6}/_{62}$), 32.3% ($^{20}/_{62}$) and 27.4% ($^{17}/_{62}$) for absent, poor, good and excellent collaterals, respectively. There were no significant differences in the prevalence of the grades of coronary collaterals in the different dominant patterns in anterior interventricular branch obstructions (p = 0.09) (Table 24).

b) CIRCUMFLEX BRANCH

The only grade of the collateral pathways in the co-dominant pattern was the poor collaterals and was recorded in two angiograms. The grades of the collateral pathways in the left dominant pattern were recorded as 10.5% ($^{2}/_{19}$), 26.3% ($^{5}/_{19}$), 47.4% ($^{9}/_{19}$) and 15.8% ($^{3}/_{19}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the right dominant pattern were recoded as 40.9% ($^{27}/_{66}$), 18.2% ($^{12}/_{66}$), 22.7% ($^{15}/_{66}$) and 18.2% ($^{12}/_{66}$) for absent, poor, good and excellent

collaterals, respectively. There was a significant difference in the prevalence of the grades of coronary collaterals in the different dominant patterns in circumflex branch obstructions ($p = 0.05$) (Table 24).

***Table 24**: Grading of the coronary collateral pathways in the different dominant patterns of the main coronary arteries.*

Coronary artery	Dominance	Grades of collateral vessel (%)				*P*-value
		Absent	Poor	Good	Excellent	
AIB	Co-dominance	33.3	66.7	-	-	0.09
	Left	27.3	18.2	45.5	9.4	
	Right	30.6	9.7	32.3	27.4	
Circumflex branch	Co-dominance	-	-	100	-	0.05
	Left	10.5	26.3	47.4	15.8	
	Right	40.9	18.2	22.7	18.2	
RCA	Co-dominance	25	-	37.5	37.5	0.01
	Left	50	-	30	20	
	Right	14.5	13	40.6	31.9	

c) RIGHT CORONARY ARTERY

The grading of the collateral pathways in the co-dominant pattern was recorded as 25% ($^{2}/_{8}$) for absent collaterals and 37.5% ($^{3}/_{8}$) for good and excellent collaterals, respectively. The grading of the collateral pathways in the left dominant pattern was recorded as 50% ($^{10}/_{20}$), 0%, 30% ($^{6}/_{20}$) and 20% ($^{4}/_{20}$) for absent, poor, good and excellent collaterals, respectively. The grading of the collateral pathways in the right dominant pattern was recorded as 14.5% ($^{20}/_{138}$), 13% ($^{18}/_{138}$), 40.6% ($^{56}/_{138}$) and 31.9% ($^{44}/_{138}$) for absent, poor,

good and excellent collaterals, respectively. There were significant differences in the prevalence of the grades of coronary collaterals in the different dominant patterns in RCA obstructions ($p = 0.01$) (Table 24).

4.7 THE EFFECT OF CORONARY COLLATERAL ARTERIES ON LEFT VENTRICULAR FUNCTION

The relationship between the development of functional coronary collateral pathways in the obstruction of the main coronary arteries and left ventricular function was evaluated. The coronary angiograms of the patients (n = 97) that had left ventriculography performed with the recording of their ejection fractions were selected for analysis (Table 25). In addition, the relationship between the location of atherosclerotic lesions observed and the ejection fraction (EF) in the patients that met the criteria was evaluated.

***Table 25**: Parameters of patients that had left ventriculography performed.*

Parameters	**Values (n=97)**			
Mean age (SD)	59.1 years (8.8 years)			
Mean ejection fraction (SD)	60.2 % (18.1%)			
Sex (%)	Female (25.8)		Male (74.2)	
Coronary dominance (%)	Co-dominance (3.1)	Left (13.4)	Right (83.5)	
Location of obstruction (%)	Proximal (45.4)	Middle (38.1)	Distal (16.5)	
Grading of collateral (%)	Absent (15.4)	Poor (15.4)	Good (36.9)	Excellent (32.3)

4.7.1 RELATIONSHIP BETWEEN ATHEROSCLEROTIC LESION LOCATION AND CORONARY COLLATERAL GRADES IN PATIENTS THAT HAD VENTRICULOGRAPHY

The grades of the collateral pathways with respect to the location of atherosclerotic obstruction were evaluated. It was recorded as 15.9% ($^{7}/_{44}$), 9.1% ($^{4}/_{44}$), 34.1% ($^{15}/_{44}$) and 40.9% ($^{18}/_{44}$) in the *proximal region* of the coronary arteries for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the

obstruction of the *middle region* were recorded as 16.2% ($^{6}/_{37}$), 16.2% ($^{6}/_{37}$), 37.8% ($^{14}/_{37}$) and 29.7% ($^{11}/_{37}$) for absent, poor, good and excellent collaterals, respectively. The grades of the collateral pathways in the obstruction of the *distal region* were recorded as 18.8% ($^{3}/_{16}$), 18.8% ($^{3}/_{16}$), 37.5% ($^{6}/_{16}$) and 25% ($^{4}/_{16}$) for absent, poor, good and excellent collaterals, respectively. There was no significant difference in the prevalence of the grades of coronary collaterals in the different regions of obstruction (p = 0.87) (Table 26).

***Table 26**: Grading of the coronary collateral pathways in the obstruction of the different regions of the main coronary arteries in patients that had left ventriculography done.*

Obstructed coronary arterial region	**Grades of collateral vessel (%)**				***P*-value**
	Absent	**Poor**	**Good**	**Excellent**	
Proximal	15.9	9.1	34.1	40.9	0.87
Middle	16.2	16.2	37.8	29.7	
Distal	18.8	18.8	37.5	25	

4.7.2 EFFECT OF ATHEROSCLEROTIC LESION LOCATION ON LEFT VENTRICULAR FUNCTION

The mean EF of the patients with the proximal, middle and distal location of atherosclerotic lesions were 63.3%, 57.8% and 57.5%, respectively (Table 27). This indicated that the best mean EF was recorded in the patients with proximally located atherosclerotic lesions. However, analysis of variance (ANOVA) showed that there was no significant difference in the mean EF calculated for the different location of atherosclerotic lesions (p = 0.33) (Table 27).

***Table 27**: Mean ejection fraction of patients in the different location of obstructive atherosclerotic lesions.*

Lesion location	Sample size (n)	Mean (%)	SD	Min (%)	Max (%)	*P*-value
Proximal	44	63.3	16	29.4	86.5	0.33
Middle	37	57.8	19.8	18.7	85.9	
Distal	16	57.5	19.5	19.2	88.4	
Total	97	60.2	18.1	18.7	88.4	

4.7.3 EFFECT OF CORONARY COLLATERAL GRADES ON LEFT VENTRICULAR FUNCTION

The mean EF of the patients with absent, poor, good and excellent coronary collaterals were calculated as 50.4%, 47%, 60.5% and 70%, respectively (Table 28). Analysis of variance (ANOVA) showed a significant difference in the mean EF calculated for the different coronary collateral grades in the patients ($p < 0.001$) (Table 28).

***Table 28**: Mean ejection fraction of patients in the different coronary collateral grades.*

Collateral grade	Sample size (n)	Mean (%)	SD	Min (%)	Max (%)	*P*-value
Absent	16	50.4	17.6	19.4	74.3	**< 0.001**
Poor	13	47	12	29.4	66.3	
Good	35	60.5	18.9	18.7	84.7	
Excellent	33	70	13.8	29.7	88.4	
Total	97	60.2	18.1	1879	88.4	

Post-hoc test was done to determine the significance of the differences in mean EF calculated for each grade of coronary collateral. There were significant differences between the mean EF calculated for patients with absent and excellent collaterals (p =

0.004) and between the mean EF for poor and excellent collaterals ($p < 0.001$) (Table 29). In addition, there was also a significant difference between the mean EF calculated for patients with poor and good collaterals ($p < 0.05$) (Table 29). The mean EF of the patients was also correlated with the coronary collaterals grades. In assessing the correlation between the mean EF and the coronary collaterals grades, a Spearman's rho correlation analysis was performed. This revealed a positive correlation coefficient (r = 0.478) that was significant ($p < 0.001$) between the mean EF of the patients and the coronary collateral grades (Table 30). This showed that the patients with better coronary collateral grade had a higher mean EF.

***Table 29**: Post-hoc test for multiple comparison of the mean ejection fraction between the different coronary collateral grades.*

(I) Collateral grade	(J) Collateral grade	Mean Difference (I-J)	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
Absent	Poor	3.3875	0.991	-12.334	19.109
	Good	-10.1239	0.362	-25.402	5.154
	Excellent	-19.5731*	0.004	-33.948	-5.199
Poor	Absent	-3.3875	0.991	-19.109	12..334
	Good	-13.5114*	0.036	-26.417	-0.606
	Excellent	-22.9606*	0.000	-34.720	-11.201
Good	Absent	10.1239	0.362	-5.154	25.402
	Poor	13.5114*	0.036	-0.606	26.417
	Excellent	-9.4492	0.121	-20.314	1.415
Excellent	Absent	19.5731*	0.004	5.199	33.948
	Poor	22.9606*	0.000	11.201	34.720
	Good	9.4492	0.121	-1.415	20.314

*The mean difference is significant at the 0.05 level

***Table 30**: Correlation between coronary collateral grades and mean ejection fraction*

			Collateral grade	Ejection fraction
Spearman's rho	Collateral grade	Correlation Coefficient	1.000	.478**
		Sig. (2-tailed)	.	.000
		N	97	97
	Ejection fraction	Correlation Coefficient	.478**	1.000
		Sig. (2-tailed)	.000	.
		N	97	97

**. Correlation is significant at the 0.01 level (2-tailed).

CHAPTER 5

DISCUSSION

5.1 SAMPLE DISTRIBUTION

The present study was conducted to identify the anatomic pathways of the coronary collaterals and to assess the morphologic parameters of the coronary arteries that may affect the development of these collateral pathways. In addition, the functional effect of the coronary collateral pathways on the left ventricle was also examined. The gross anatomical features of the coronary angiograms used in this study were macroscopically similar to the currently accepted description of coronary arterial vasculature in standard anatomical textbooks (Sinnatamby, 2006; Snell, 2008; Standring *et al*., 2008) and clinical textbooks (Allen *et al*., 2000; Topol *et al.*, 2002; Townsend *et al*., 2004; Bonow *et al*., 2011).

The available literature is replete with studies dedicated to coronary arteries applying a dynamic approach in appreciating aspects of their morphology, function and pathology. This study focused primarily on the anatomic and functional characteristics of the coronary collateral pathways that are of clinical interest in patients with total coronary arterial obstruction(s). The mean age of the female patients (63.9 years) in the analyzed angiograms was significantly higher than that of males (57.4 years) ($p < 0.001$). The findings of the present study corroborated earlier reports that males develop coronary artery disease seven to 10 years earlier than females (Maas and Appelman, 2010). According to Maas and Appelman (2010), the exposure to endogenous oestrogen delays the manifestation of coronary artery disease in females and they are consequently less likely to be referred for coronary angiography (Schenck-Gustafsson, 1996). Therefore, in patients presenting with symptomatic MI, females are usually older than males (Saleh *et al*., 2013).

5.2 CORONARY ARTERY MORPHOLOGY

The LCA normally arises from the left aortic sinus and functions mainly as a conduit to its terminal branches, which are the anterior interventricular branch, circumflex branch and RM artery (when present). The LCA usually has no branches before its division into its terminal branches, but may give off a small atrial ramus and rarely, the SA nodal artery (Standring *et al*., 2008). The present study did not record any branch from the LCA before its division into its terminal branches. In the present study, the bifurcation of the LCA into anterior interventricular branch and circumflex branch was the most prevalent branching pattern (91%), followed by trifurcation of the LCA (8.7%), while the least recorded branching pattern was the quadrifurcation of the LCA (0.3%). The findings of this study corroborated previous reports on the branching patterns of the LCA (Rieg and Petit, 2004; Lujinović *et al.,* 2005; Kilic and Kirici, 2007; Kosar *et al.*, 2009; Christensen *et al*., 2010; Ajayi *et al*., 2013c).

With respect to coronary arterial dominance, the present study recorded it as 82.9%, 12.9% and 1% for right, left and co-dominance, respectively. This dominant pattern compared favourably with the results of Nerantzis *et al*., (1996) (89%, 10% and 1%), Christensen *et al*., (2010) (85.7%, 9.5% and 4.8%) and Ajayi *et al*., (2013c) (81.5%, 15.2%, and 3.3%) for right, left and co-dominance, respectively. However, it differed with the findings of Kurgia *et al*., (1986) (46%, 40% and 14%) and Mian *et al*., (2011) (60.5%, 19.5% and 20%) for right, left and co-dominant patterns, respectively.

5.3 DISTRIBUTION OF OBSTRUCTIVE ATHEROSCLEROTIC LESIONS

(a) Type of obstructive vessel disease

The presence of obstructive atherosclerotic lesions in the main coronary arteries (anterior interventricular branch, circumflex branch and RCA) resulting in single, double and triple vessel obstructive disease patterns were recorded in 86%, 12.9% and 1% of the angiograms analyzed, respectively. The presence of single, double and triple vessel obstructive disease were recorded as follows: anterior interventricular branch (69.7%, 26.3% and 3.9%); circumflex branch (71.3%, 25.3% and 3.4%) and RCA (78.9%, 19.3% and 1.8%) (Figure 38; Page 76). From the literature reviewed, there are no reports on the prevalence of the types of obstructive atherosclerotic lesions in the main coronary arteries. This may be due to the fact that most of the previous studies assessed coronary arterial stenosis rather that total coronary arterial occlusion.

However, in a study by Mock *et al*. (1982) on the short-term survival of patients with coronary artery disease using the Coronary Artery Surgery Study (CASS) registry, it was reported that cumulative survival for patients with single, double and triple vessel disease was 92%, 84% and 68%, respectively. In another study, Emond *et al*. (1994) showed that the long-term survival of patients with single, double and triple vessel disease was 74%, 59% and 40%, respectively. Proudfit *et al.* (1983) reported the fifteen-year survival rates in patients with obstructive coronary artery disease as 48%, 28% and 18% for single, double and triple vessel disease, respectively. In addition, sudden death of patients with coronary artery disease was significantly associated with coronary artery occlusion

(Trappe *et al*., 1989). These studies indicated the better survival of patients with single vessel disease when compared to other types of vessel diseases. The highest prevalence of patients with single obstructive vessel disease in the current study may be explained by their better survival (short-term or long-term) when compared to other obstructive vessel diseases.

(b) Location of atherosclerotic lesions

Atherosclerotic lesions were found in the *proximal regions* (Page 68) of the anterior interventricular branch (63.2%), circumflex branch (46%) and RCA (41.6%) of the angiograms with obstructive vessel disease. The obstructive lesions were found in the *middle regions* of the anterior interventricular branch (34.2%), circumflex branch (34.5%) and RCA (39.2%) of the angiograms, while the obstruction of the *distal regions* was found in the anterior interventricular branch (2.6%), circumflex branch (19.5%) and the RCA (19.3%) in the angiograms analyzed (Figures 39 - 41). In the present study, the proximal location of obstructive lesion was found to be highest in the anterior interventricular branch; this corroborated the only report on the location of obstructive atherosclerotic lesions from the literature reviewed by Tatli *et al*. (2007). In their study, they reported on the presence of atherosclerotic lesions in the anterior interventricular branch and the RCA in 74 patients with exclusively single vessel obstructive disease. The study documented proximally located obstructive lesions in 62% and 38% of these patients in anterior interventricular branch and RCA, respectively.

Ajayi *et al*., (2013b) reported that the morphology of the LCA influences the development and location of atherosclerotic lesions in its branches. In their study, it was shown that the longer the LCA, the more proximally located are atherosclerotic lesions in its branches (anterior interventricular branch and circumflex branch). The present study also confirmed previous reports that atherosclerotic lesions are preferentially situated at the proximal region of daughter vessels (Asakura and Karino, 1990; Park and Park**,** 2009). In the present study, atherosclerotic lesions were found to be highest in the proximal region of the anterior interventricular branch (63.2%), and then followed by the circumflex branch (46%). These are branches of the LCA and it has been reported that the proximal lateral walls of daughter branches are sites of low flow and low shear stress (Caro, 2009) with an increased tendency for atherosclerotic lesion generation (Gibson *et al*., 1993; Scher, 2000). Therefore, the least prevalence of proximally located lesions in the main coronary arteries found in the RCA (41.6%) may have resulted from the fact that it is less exposed to low shear at its proximal region than the anterior interventricular branch and circumflex branch.

5.4 ANATOMIC PATHWAYS OF CORONARY COLLATERALS IN TOTAL CORONARY ARTERIAL OBSTRUCTIONS

In routine coronary angiographic reports, the precise location of atherosclerotic lesions is often not stated. In addition, the presence or absence of coronary collaterals is not usually indicated. However, as shown earlier in the review of the literature (Pages 41-53), several authors have used various terminologies for the coronary collaterals. Some of these terminologies include: inter-arterial, bridging, trans-arterial, septal, ventricular free wall and bypass arteries. The most extensive description of these collaterals was by Levin (1974) who also attempted to identify the regions of origin and termination of the collaterals in the main coronary arteries. The present study identified the precise origin and termination of the coronary collaterals by using the coronary arterial segments described by the BARI study group. With the use of the coronary artery segments for the origin and termination of the coronary collateral, the confusion that may arise from the use of various terminologies for the same structure will be eliminated.

The present study recorded more collateral pathways than the report of Levin (1974) who recorded seven, five and 10 collateral pathways for the anterior interventricular branch, circumflex branch and the RCA obstructions, respectively. In the obstruction of the anterior interventricular branch, circumflex branch and the RCA in the present study, 32, 46 and 37 different coronary collateral pathways were documented, respectively (Tables 17-19). Therefore, there was a major difference in the number pathways for the coronary collateral arteries in the present study and the report of Levin (1974). The present study recorded the existence of numerous pathways for the coronary collaterals and was able to

identify segments of origin and termination of these arteries. Improvement in the identification and labelling of these collaterals channels will be of immense benefit during coronary angiographic reporting in order to determine the significance of their presence. The presence of several collateral pathways in the obstructions of the main coronary artery indicated that these pathways existed as microvessels in the heart (Rockstroh and Brown, 2002). These microvessels subsequently developed into angiographically demonstrable vessels (Levin, 1974) by hypertrophic evolution (Koerselman *et al*., 2003) following coronary arterial obstruction. In the sequel to the occlusion of the coronary arteries, there is reduction in coronary collateral vascular resistance with an increase in coronary collateral vascular flow (Tatli *et al*., 2007).

It was observed that in the obstructions of the main arteries in the present study, a large number of the coronary collaterals were from the proximal region of the obstructed artery or its branches. In anterior interventricular branch, circumflex and RCA obstructions, 37.5%, 50% and 43.2% were from the proximal regions of these arteries or their branches (Table 20). It was also noted that in the obstruction of the circumflex branch and the RCA, most of the collaterals were from the circumflex branch. This showed that coronary collaterals are better developed on the inferior surface of the heart because these two vessels (circumflex branch and the RCA) are closer to each other on the inferior myocardial surface. Since the foundation for the collateral network were laid down during embryogenesis (Loukas *et al*., 2009a), the findings of the present study indicated that most of the collaterals to the distal region of an obstructed artery were recruited from the closest interconnecting arterioles. Collaterals develop through arteriogenesis (Meier *et*

al., 2013) which leads to the maturation of pre-existing interconnecting arterioles after arterial occlusion (Cai and Schaper, 2008).

The high success rate achieved in the retrograde approach to the site of obstruction in retrograde angioplasty has made it a safe and effective procedure in the management of patients with CTO of the coronary arteries (Fernández-Díaz *et al*., 2010). The retrograde access to the point of occlusion may be through epicardial or septal collaterals: However, the septal collaterals are preferred (Sumerly *et al*., 2007; Fernández-Díaz *et al*., 2010). The identification of the coronary collateral pathways is very important during retrograde angiogplasty (Ozawa, 2006). Therefore, it is essential to define these pathways in the subset of patients that may benefit from retrograde angioplasty.

5.5 GRADES OF THE CORONARY COLLATERALS IN THE OBSTRUCTIONS OF THE CORONARY ARTERIES

The richest collateral supply was to the RCA with a prevalence of excellent collaterals of 30.7% recorded in its obstructions; this was followed by the anterior interventricular branch (23.7%), and the least was in circumflex branch (17.2%) (Figure 42; Page 123). The result of the present study confirmed previous reports that coronary collateral arteries are better developed in patients with RCA obstructions than in obstructions of other coronary vessels (Ilia *et al.*, 1997; Tatli *et al*., 2007 and Sun *et al*., 2013). Therefore, it may be deduced that the quality of coronary collaterals developed is dependent on the morphology of the obstructed coronary artery and collateralization from other vessels (Sun *et al*., 2013).

5.5.1 GRADES OF CORONARY COLLATERALS IN RELATION TO AGE

With respect to the influence of age on coronary artery collateral development, the prevalence of excellent collaterals was higher in the patients > 60 years of age than in those ≤ 60 years of age (32.3% *vs* 17.9%) in the anterior interventricular branch obstructions. This is contrary to the findings of the prevalence of excellent collaterals (10.5% *vs* 25%) and (22.1% *vs* 39.3) for the patients > 60 years and those ≤ 60 years age in the circumflex branch and RCA obstructions, respectively. However, there was no statistically significant difference in the prevalence of excellent coronary collateral arteries in coronary arteries examined. Therefore, the present study found no association between patients' age and the development of excellent or well-functioning collaterals.

The result of the present study corroborated the finding of Fujita *et al*. (1999) who also used a cut-off age of 60 years and reported that the extent of coronary collateral development was similar in patients regardless of their age. Furthermore, van der Hoeven *et al.* (2013) in their study divided patients into two groups (≤64 years and ≥65 years) and also found no association between higher age and the development of poor collaterals. Conversely, it differed from the reports of Nakae *et al.* (2000) and Sun *et al*. (2013) who stated that well-developed collaterals were significantly lower in patients older than > 65 years of age. The disparity in the results may be explained by the difference in the methods of coronary collateral assessment and grading of these channels. In addition, Cohen *et al*. (1989) suggested the likelihood of genetic predisposition to the development of functional coronary collaterals because these anastomotic channels are laid down in utero.

5.5.2 GRADES OF CORONARY COLLATERALS IN RELATION TO SEX

In the present study, the prevalence of excellent collaterals was higher in males in the obstructions of the main coronary arteries (Table 22; Page 130). However, there was no statistically significant difference in the prevalence of excellent collaterals between males and females; therefore, there was no association between the patients' sex and the development of excellent collaterals. Although, the present finding differed from the report of Sun *et al*. (2013) who stated that well-developed collaterals was significantly lower in female patients, it confirmed the reports of Fujita *et al*. (1999) and Nakae *et al.* (2000) who also found no significant difference.

5.5.3 GRADES OF CORONARY COLLATERALS IN RELATION TO ATHEROSCLEROTIC LESION LOCATION IN THE ANALYZED ANGIOGRAMS

In the study by Piek *et al*. (1997), the proximal location of atherosclerotic lesion was reported to be a significant predictor of the development of coronary collateral arteries. They stated that the "*proximal location will result in a lower threshold for the development of myocardial ischemia owing to the larger size of the myocardium "at risk" and, hence, to the stimulation of collateral vascular development*". The current study also found a significant association between the development of excellent collaterals and the proximal location of lesion in the RCA. However, in the anterior interventricular branch and circumflex branch, no significant association was recorded with respect to the location of atherosclerotic lesions (Table 23; Page 134).

5.5.4 GRADES OF CORONARY COLLATERALS IN RELATION TO CORONARY ARTERIAL DOMINANCE

From the literature reviewed, it is apparent that there are no reports on the influence of coronary arterial dominance on development of functional coronary collaterals. In the present study, the prevalence of excellent coronary collaterals was higher in patients with right coronary arterial dominant pattern than in the left dominant pattern (Table 24; Page 136). A significant association was found between right coronary arterial dominant pattern and the development of excellent coronary collaterals in circumflex branch and RCA obstructions. The higher prevalence of excellent collaterals found in the right dominant pattern may be related to the fact noted earlier that coronary collaterals are better developed on the inferior surface of the heart. With the RCA also contributing in

the blood supply to the LV in the right dominant pattern, the development of excellent collaterals may be amplified by this coronary arrangement. Therefore, this morphological pattern of the coronary arterial tree has a significant effect on coronary collateral development.

5.6 PROPOSED ALGORITHM FOR THE LABELLING OF THE CORONARY COLLATERAL ARTERIES

As noted earlier in the review of literature, the functional importance of the coronary collaterals has been controversial (Traupe *at al*., 2010) due to the lack of a reference method for determining these arteries (Wainwright *et al*., 1980; Baroldi *et al*., 2005). The lack of a unified system for the assessment and labelling of these coronary collateral channels had resulted in difficulty in communication amongst clinicians and researchers (Loukas *et al*., 2009). Some authors have identified the anatomic pathways of the coronary collaterals using various terminologies (May, 1960; Paulin, 1967; Levin, 1974), while others have functionally graded the coronary collaterals (Wainwright *et al*., 1980; Rentrop *et al*., 1985; Seiler *et al*., 2001; Werner *et al*., 2003).

The present study proposes an algorithm for identifying and labelling the coronary collateral pathways. The proposed algorithm combines the anatomic and functional properties of the coronary collateral pathways. In addition, it identifies the specific segments of origin and termination of the coronary collateral arteries by using the BARI coronary map. It is envisaged that the proposed algorithm will result in a comprehensive and unified system of coronary angiographic image reporting in the obstruction of the coronary arteries with or without the development of coronary collaterals. An example of a proposal is as follows:

1. ***AIB$_{12}$; 17-13; Gr 3***, *which can be interpreted as the* ***obstruction of the*** **anterior interventricular branch** ***in segment 12 that has a collateral origin from segment 17 and terminating at segment 13 with a grade of 3*** (Plate 1; Page 83).

2. ***AIB_{12}; RV-14; Gr 2***, *which can be interpreted as the* ***obstruction of the anterior interventricular branch in segment 12 that has a collateral origin from right ventricular branch of the RCA and terminating at segment 14 with a grade of 2*** (Plate 3; Page 85).
3. ***Cx_{18}; 5-19a; Gr 3***, *which can be interpreted as the* ***obstruction of the circumflex branch in segment 18 that has a collateral origin from segment 5 and terminating at segment 19a with a grade of 3*** (Plate 13; Page 98).
4. ***Cx_{19a}; 21-23; Gr 2***, *which can be interpreted as the* ***obstruction of the circumflex branch in segment 19a that has a collateral origin from segment 21 and terminating at segment 23 with a grade of 2*** (Plate 15; Page 102).
5. ***RCA_1; CB-RV; Gr 2***, *which can be interpreted as the* ***obstruction of the RCA in segment 1 that has a collateral origin from the conal branch of RCA and terminating at the right ventricular branch of RCA with a grade of 2*** (Plate 18; Page 108).
6. ***RCA_2; 17-9; Gr 2***, *which can be interpreted as the* ***obstruction of the RCA in segment 2 that has a collateral origin from segment 17 and terminating at segment 9 with a grade of 2*** (Plate 21; Page 112) .

5.7 THE EFFECT OF CORONARY COLLATERAL VESSELS ON LEFT VENTRICULAR FUNCTION

The relationship between the development of functional coronary collateral pathways in the obstruction of the main coronary arteries and left ventricular function was evaluated in the patients that had left ventriculography performed during angiography. It was observed that in the angiograms reviewed, ventriculography was routinely done only by some of the Cardiologists. However, other Cardiologists either selectively perform ventriculography during coronary catheterization or do not. Perhaps, LV function was assessed through other modalities such as echocardiography by these Cardiologists that do not perform ventriculography. This may have accounted for the low number of patients that had left ventriculography (n=97) in the angiograms that were selected for analysis in this series. Therefore, if ventriculography was routinely performed by all the Cardiologists in the angiograms reviewed, it would have been easier to determine the effect of coronary arterial obstruction on left ventricular function in this set of patients. Subsequently, the impact of coronary collateral development on left ventricular function in these patients may also be ascertained.

5.7.1 RELATIONSHIP BETWEEN ATHEROSCLEROTIC LESION LOCATION AND CORONARY COLLATERAL GRADES IN PATIENTS THAT HAD VENTRICULOGRAPHY

Coronary collateral arterial development represents a compensatory mechanism (Khoo *et al*., 2014) triggered by myocardial ischemia due to coronary atherosclerosis (Matsunaga *et al*., 2000; Chilian *et al*., 2012). The development of coronary collaterals has also been attributed to the increase in pressure gradient between the normal and obstructed coronary arteries (Schaper, 2009). The pressure gradient causes increased blood flow in the coronary collateral vascular bed (Tatli *et al*., 2007) with the resultant increased fluid shear stress and activation of endothelium and growth factors (Schaper, 2009). Furthermore, the pressure gradient is dependent on the severity of coronary artery stenosis (van der Hoeven *et al.*, 2013).

In the present study, the highest prevalence of excellent collaterals in patients who had ventriculography performed was recorded in those with proximally located lesions (40.9%). Excellent collaterals were found in 29.7% and 25% of middle and distally located lesions, respectively. The proximal location of atherosclerotic lesion will result in an increased drop in the pressure gradient between the normal (collateral donating) coronary artery and the obstructed (collateral receiving) vessel. In addition, the proximal location of the atherosclerotic lesion is associated with an increase in myocardial tissue 'at risk' of ischemia (Piek *et al*., 1997). Fujita *et al*., 1999 stated that the functional ability of the coronary collaterals is influenced by the efficiency of collateral vessel recruitment sequel to the development of a pressure gradient across the collateral network. Therefore, the highest prevalence of excellent collaterals in patients with proximally located lesions

in the present study may have resulted from the combination of these factors (increased pressure gradient and myocardial ischemia).

5.7.2 EFFECT OF ATHEROSCLEROTIC LESION LOCATION ON LEFT VENTRICULAR FUNCTION

From the literature reviewed, it is apparent that there are no reports on the relationship between atherosclerotic lesion location and left ventricular function. In the present study, the mean EF calculated for the patients with a proximally located lesion was the highest (63.3%) as compared to mean EF for the middle (57.8%) and distally (57.5%) located lesions. This may have resulted from the fact that the patients with proximally located lesions had the highest prevalence of excellent collateral arteries. Therefore, the proximal location of an atherosclerotic lesion influences collateral vessel development with resultant positive effect on left ventricular function preservation.

5.7.3 EFFECT OF CORONARY COLLATERAL GRADES ON LEFT VENTRICULAR FUNCTION

As stated in the review of literature, there are conflicting reports with respect to the functional importance of coronary collateral arteries (Pages 59-62). Sheehan *et al*. (1987) examined the global left ventricular ejection fraction (LVEF) in patients with acute MI before treatment and at discharge. They reported that the global LVEF increased in patients with collaterals but was the same in patients without coronary collaterals. Habib *et al*. (1991) divided patients who failed to canalize at 90 minutes after administration of a thrombolytic agent into two groups (with and without collaterals) and reported that

global LVEF was significantly greater in patients with coronary collaterals at hospital discharge. On the contrary, Wackers *et al*. (1989) found no difference in the global LVEF in patients with and without coronary collaterals.

From the literature reviewed, the present study appears to be the first to evaluate in detail the relationship between the different grades of coronary collateral arteries and LVEF in the presence of total coronary arterial obstruction. There was a significant difference ($p < 0.001$) in the mean EF calculated for the different grades of coronary collaterals. In addition, post-hoc test showed a significant difference in the mean EF between excellent and absent collaterals ($p = 0.004$) and excellent and poor collaterals ($p < 0.001$). Thus, the development of excellent collaterals has a significant supportive effect on the preservation of left ventricular function as compared to patients with absent or poor collateralization. There was also a significant positive correlation between coronary collateral grades and mean EF calculated for the different collateral grades. The present study corroborated the findings of Sheehan *et al*. (1987) and Habib *et al*. (1991) that the presence of excellent and well-functioning coronary collaterals has a significant role in the preservation of left ventricular function.

In addition, the present study showed that, as the grades of coronary collaterals increased, there was an improvement in the ability of these collaterals to preserve left ventricular function. Consequently, left ventricular myocardial perfusion was greater in patients with well-developed coronary collaterals and resulted in a better recovery of left ventricular function in the presence of myocardial ischemia or MI.

Vanker *et al*. (2014) reported that anatomical variations of the coronary arteries such as the intra-myocardial course of anterior interventricular branch may present the surgeon with technical challenges during coronary artery bypass graft surgery. Therefore, the presence of morphological variation of the coronary arteries may affect the technique employed during surgical intervention and the subsequent outcome. To date, the surgical significance of collateral circulation has not yet been properly investigated. However, it has been reported that the collateral circulation is favorable for the successful construction of coronary artery bypass grafts (Levin 1974). From the result of the present study, it may be deduced that the presence of well-development collaterals may influence decision making in the management of patients with coronary arterial obstruction. In the presence of an adequately preserved left ventricular function by coronary collaterals in asymptomatic patients, there may be no need for coronary angioplasty, stent insertion or surgical intervention. Anecdotal reports have also shown that patients with total coronary arterial obstruction who had developed functional coronary collateral arteries took part in sporting activities. The identification of coronary collateral arteries during coronary catheterization may require further evaluation of their functional importance with modalities such as CFI or MCE. Therefore, the significance of the coronary collateral arteries should not be underestimated.

CHAPTER 6

CONCLUSION

6.1 SAMPLE DISTRIBUTION

The gross anatomical features of the coronary angiograms used in this study corroborated the description of coronary arterial vasculature in standard anatomical textbooks (Sinnatamby, 2006; Snell, 2008; Standring *et al*., 2008) and clinical textbooks (Allen *et al*., 2000; Topol *et al.,* 2002; Townsend *et al*., 2004; Bonow *et al*., 2011). The mean age of the female patients (63.9 years) in the analyzed angiograms was significantly higher than that of males (57.4 years) ($p < 0.001$). Therefore, in patients undergoing angiography for symptomatic MI, females are usually older than males (Saleh *et al*., 2013).

6.2 CORONARY ARTERY MORPHOLOGY

The bifurcation of the LCA into anterior interventricular branch and circumflex branch was the most prevalent branching pattern (91%), followed by trifurcation of the LCA (8.7%), while the least branching pattern was the quadrifurcation of the LCA (0.3%). Right coronary arterial dominance had the highest prevalence in the present study (82.9%) and the left and co-dominant patterns were 12.9% and 1%, respectively. This dominant pattern compares favorably with the some of the previous results on coronary arterial dominance (Nerantzis *et al*., 1996; Christensen *et al*., 2010; Ajayi *et al*., 2013c).

6.3 DISTRIBUTION OF OBSTRUCTIVE ATHEROSCLEROTIC LESIONS

The presence of obstructive atherosclerotic lesions in the main coronary arteries (anterior interventricular branch, circumflex branch and RCA) resulting in single, double and triple vessel obstructive disease patterns were recorded in 86%, 12.9% and 1% of the angiograms analyzed, respectively. The present finding confirms earlier reports that the short-term and long-term survival of patients with coronary artery disease was best in those with single vessel disease.

The present study also confirmed previous reports that atherosclerotic lesions are preferentially situated at the proximal region of daughter vessels. The lesions were found to be highest in the proximal region of the anterior interventricular branch (63.2%), and then followed by the circumflex branch (46%). These are branches of the LCA and it has been reported that the proximal lateral walls of daughter branches have an increased tendency for atherosclerotic lesion generation. The least prevalence of proximally located atherosclerotic lesions recorded in the RCA (41.6%) may due to the fact that it is less exposed to low shear stress than the anterior interventricular branch and the circumflex branch.

6.4 ANATOMIC PATHWAYS OF CORONARY COLLATERALS IN TOTAL CORONARY ARTERIAL OBSTRUCTIONS

The present study identified the precise origin and termination of the coronary collaterals by using the BARI coronary arterial segments. The confusion that may arise from the use of various terminologies for the same structure will be eliminated when the coronary artery segments are used for the origin and termination of the coronary collateral. The present study documented 115 different coronary collateral pathways which was higher that the most extensive study in the literature reviewed on collateral pathways by Levin (1974) who recorded 26 collateral pathways.

6.5 GRADES OF THE CORONARY COLLATERALS IN THE OBSTRUCTIONS OF THE CORONARY ARTERIES

The richest collateral supply was to the RCA with 30.7% prevalence of excellent collaterals, and the least was in circumflex branch (17.2%). This confirmed previous reports that coronary collateral arteries are better developed in patients with RCA obstructions than in obstructions of other coronary vessels. The present study found no significant association between patients' age and the development of excellent or well-functioning collaterals. There was also no significant association between the patients' sex and the development of excellent collaterals.

The current study found a significant association between the development of excellent collaterals and the proximal location of lesion in the RCA. However, in the anterior interventricular branch and circumflex branch, no significant association was recorded

with respect to the location of atherosclerotic lesions. The prevalence of excellent coronary collaterals was higher in patients with right than in left coronary arterial dominant pattern. A significant association was recorded between right coronary arterial dominance and the development of excellent collaterals in the circumflex branch and the RCA. Therefore, coronary collateral arteries are better developed on the inferior myocardial surface due to this coronary arterial arrangement. It may be concluded that coronary arterial morphological pattern influences coronary collateral artery development.

6.6 PROPOSED ALGORITHM FOR THE LABELLING OF THE CORONARY COLLATERAL ARTERIES

An algorithm is proposed in the present study for identifying and labelling the coronary collateral pathways. The proposed algorithm combines the anatomic and functional properties of the coronary collateral pathways. It is envisaged that this algorithm will contribute to reporting of coronary angiographic image in the obstruction of the coronary arteries.

6.7 THE EFFECT OF CORONARY COLLATERAL VESSELS ON LEFT VENTRICULAR FUNCTION

The highest prevalence of excellent collaterals was recorded in those with proximally located lesions (40.9%). Excellent collaterals were found in 29.7% and 25% of middle and distally located lesions, respectively. The highest prevalence of excellent collaterals in patients with proximally located lesions in the present study may have resulted from the combination of the effects of increased pressure gradient and myocardial ischemia.

The mean EF calculated for the patients with proximally located lesions was the highest (63.3%) as compared to mean EF for the middle (57.8%) and distally (57.5%) located lesions. This may have resulted from the fact that the patients with proximally located lesions had the highest prevalence of excellent collateral arteries. Therefore, the proximal location of atherosclerotic lesion influences collateral vessel development with resultant positive effect on the preservation of left ventricular function.

There was a significant difference ($p < 0.001$) in the mean EF calculated for the different grades of coronary collaterals with the highest mean EF recorded for excellent collateralization. There was also a significant positive correlation between coronary collateral grades and mean EF. Therefore, the present study showed that, as the grades of coronary collaterals increased, there was an improvement in the ability of these collaterals to preserve left ventricular function.

6.8 STUDY LIMITATIONS

The limitation of the present study are: The absence of clinical records in terms the duration of the obstructive lesion in the patients made it difficult to determine if they were acute or chronic. In addition, it was not possible to determine patients with risk factors and co-morbid conditions such as diabetes mellitus and hypertension that may influence collateral vessel development. This would have enhanced the study; however, it was not possible because the study protocol was only designed for the use of angiographic records and not the clinical records of the patients. Furthermore, conventional coronary angiography is incapable of visualizing coronary collateral vessels with a diameter less than 100µm (Nakae *et al*., 2000). The evaluation of these very tiny collateral channels may be better with the use of MCE (Mills *et al*., 2000) or CFI measurement (Meier *et al*., 2013). However, the angiographic method of grading the coronary collateral flow is still the standard of reference in the clinical environment (Fujita *et al*., 1999). Since the aim of this study was to classify the coronary collateral pathways and identify factors that affect their development, the angiographic approach appears adequate for this purpose.

REFERENCES

JOURNALS

Abaci A, Oguzhan A, Kahraman S, Eryol NK, Ünal S, Arinç H, Ergin A (1999) Effect of Diabetes Mellitus on Formation of Coronary Collateral Vessels. *Circulation* 99:2239-2242

Ajayi NO, Lazarus L, Vanker EA, Satyapal KS (2013a) The prevalence and clinical importance of an "additional" terminal branch of the left coronary artery. *Folia Morphol* 72(2):128–131

Ajayi NO, Lazarus L, Vanker EA, Satyapal KS (2013b) The impact of left main coronary artery morphology on the distribution of atherosclerotic lesions in its branches. *Folia Morphol* 72(3):197–201

Ajayi NO, Lazarus L, Vanker EA, Satyapal KS (2013c) Anatomic parameters of the left coronary artery: An angiographic study in a South African population. *Int J Morphol* 31(4):1393-1398

Ajayi NO, Lazarus L, Vanker EA, Satyapal KS (2014) Absent Left Main Coronary Artery with Variation in the Origin of its Branches in a South African Population *Anat Histol Embryol* doi: 10.1111/ahe.12109

Alderman EL, Stadius M (1992) The angiographic definitions of the Bypass Angioplasty Revascularization Investigation. *Coronary Artery Disease* **3(12)**:1189-1207

Ando K, Nakajima Y, Yamagishi T, Yamamoto S, Nakamura H (2004) Development of proximal coronary arteries in quail embryonic heart: Multiple capillaries penetrating the aortic sinus fuse to form main coronary trunk. *Circ Res* **94**:346–352

Annex BH, Simons M (2005) Growth factor-induced therapeutic angiogenesis in the heart:protein therapy. *Cardiovasc Res* **65**: 649– 655

Asakura T, Karino T (1990) Flow patterns and spatial distribution of atherosclerotic lesions in human coronary arteries. *Circ Res* **66**: 1045–1066.

Banerjee AK, Madan Mohan SK, Ching GWK, Singh SP (1993) Functional significance of coronary collateral vessels in patients with previous 'Q' wave infarction: relation to aneurysm, left ventricular end diastolic pressure and ejection fraction. *Int J Cardiol* **38**:263–71.

Baroldi G, Mantero O, Scomazzoni G (1956) The Collaterals of the Coronary Arteries in Normal and Pathologic Hearts *Circ Res* **4**:223-229

Baroldi G, Bigi R, Cortigiani L (2005) Ultrasound imaging versus morphopathology in cardiovascular diseases. Coronary collateral circulation and atherosclerotic plaque. *Cardiovasc Ultrasound* **3**:6.

Baumgartner L (1932) Leonardo da Vinci as a Physiologist. *Annals of Medical History* **4(2):** 155-171

Bernanke DH, Velkey JM (2002) Development of the coronary blood supply: Changing concepts and current ideas. *Anat Rec* **269**: 198–208.

Berry C, Balachandran KP, L'Allier PL, Lespérance J, Bonan R, Oldroyd KG (2007) Importance of collateral circulation in coronary heart disease. *Euro Heart J* **28**:278–291

Bhimalli S, Dixit D, Siddibhavi M and Shirol VS (2011) A Study Of Variations in Coronary Arterial System in Coronary artery diseaseaveric Human Heart. *World Journal Of Science And Technology* **1(5)**: 30-35

Bogers AJ, Gittenberger-de Groot AC, Poelmann RE, Peault BM, Huysmans HA (1989) Development of the origin of the coronary arteries, a matter of ingrowth or outgrowth? *Anat Embryol (Berl)* **180**: 437–441

Buschmann I, Schaper W. (2000) The pathophysiology of the collateral circulation (arteriogenesis). *J Pathol* **190**: 338– 42.

Cai W, Schaper W (2008) Mechanisms of arteriogenesis. *Acta Biochim Biophys Sin* **40(8)**: 681-692

Cankaya, B., Kantarci M., Yalcin A., Karakaya A., **Yuce I** (2009) Absence of the left main coronary artery: MDCT coronary angiographic imaging. *Eurasian J Med* **41**: 56–58.

Carmeliet P (2000) Mechanisms of angiogenesis and arteriogenesis. *Nat Med* **6 (3)**: 389-395

Caro CG. (2009) Discovery of the Role of Wall Shear in Atherosclerosis. *Arterioscler Thromb Vasc Biol* **29(2)**:158-61.

Chilian WM, Penn MS, Pung YF, Dong F, Mayorga M , Ohanyan V, Logan S, Yin L (2012) Coronary collateral growth—Back to the future. *J Mol Cell Cardiol* **52**: 905-911

Chittenden TW, Sherman JA, Xiong F, Hall AE, Lanahan AA, Taylor JM, Duan H, Pearlman JD, Moore JH, Schwartz SM, Simons M (2006) Transcriptional profiling in coronary artery disease: indications for novel markers of coronary collateralization. *Circulation* **114**:1811–1820

Choi JH, Chang SA, Choi JO, Song YB, Hahn JY, Choi SH, Lee SC, Lee SH, Oh JK, Choe Y, **Gwon HC** (2013) Frequency of myocardial infarction and its relationship to angiographic collateral flow in territories supplied by chronically occluded coronary arteries. *Circulation* **127**(6):703-709. [doi:10.1161/CIRCULATIONAHA.112.092353]

Christensen KN, Harris SR, Froemming AT, Brinjikji W, Araoz P, Asirvatham SJ, Lachman N (2010) Anatomic assessment of the bifurcation of the left main coronary artery using multidetector computed tomography. *Surg Radiol Anat* **32**: 903–909

Cohen M, Rentrop KP (1986) Limitation of myocardial ischemia by collateral circulation during sudden controlled coronary artery occlusion in human subjects: a prospective study. *Circulation.*; 74:469-476

Cohen M, Sherman W, Rentrop KP, Gorlin R (1989) Determinants of collateral filling observed during sudden controlled coronary artery occlusion in human subjects. *J Am Coll Cardiol* **13**:297–303

Conway EM, Collen D, Carmeliet P (2001) Molecular mechanisms of blood vessel growth *Cardiovasc Res* **49**:507–521

de Marchi SF, Oswald P, Windecker S, Meier B, Seiler C (2005) Reciprocal relationship between left ventricular filling pressure and the recruitable human coronary collateral circulation. *Eur Heart J* **26**: 558-566

Demer LL, Gould KL, Goldstein RA, Kirkeeide RL. (1990) Noninvasive Assessment of Coronary Collaterals in Man by PET Perfusion Imaging. *J NucI Med* **31:**259-270

Demirbag R, Yilmaz R (2005) Effects of the shape of coronary arteries on the presence, extent, and severity of their disease. *Heart Vessels* **20**:224–229

Dvir D, Kornowski R, Gurevich J, Orlov B, Aravot D (2003) Degrees of Severe Stenoses in Sigma-Shaped Versus C-Shaped Right Coronary Arteries. *Am J Cardiol* **92**:294–298

Edwards JC, Burnsides C, Swarm RL, Lansing AJ (1956) Arteriosclerosis in the intramural and extramural portions of coronary arteries in the human heart. *Circulation* 13:235–241.

Emond M, Mock MB, Davis KB, Fisher LD, Holmes DR, Chaitman BR, Kaiser GC, Alderman E, Killip T (1994) Long-term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. *Circulation* **90**:2645-2657

Fazliogullari Z, Karabulut A K, Unver Dogan N, Uysal I I (2010) Coronary artery variations and median artery in Turkish coronary artery diseaseaver hearts. *Singapore Med J* **51**: 775

Fernández-Díaz JA, Goicolea-Ruigómez J, García-Touchard A, Oteo-Domínguez JF, Domínguez-Puente JR. (2010) Retrograde Angioplasty: An Option for Total Coronary Artery Occlusions. *Rev Esp Cardiol* **63(4)**:483-7

Fiss DM (2007) Normal coronary anatomy and anatomic variations. *Supplement to Applied Radiology* 14-26

Fujita M, Nakae I,Kihara Y, Hasegawa K, Nohara Y, Ueda K, Tamaki S, Otsuka K, Sasayama S (1999) Determinants of Collateral Development in Patients with Acute Myocardial Infarction *Clin Cardiol* **22**: 595-599

Gaze DC (2013) Introduction to Ischemic Heart Disease, Ischemic Heart Disease, ISBN: 978-953-51-0993-8, *InTech*, DOI: 10.5772/55248

Gensini GG and Bruto da Costa BC (1969) The coronary collateral circulation in living man. *Am J Cardiol* **24**: 393- 400

Gibson CM, Diaz L, Kandarpa K, Sacks FM, Pasternak RC, Sandor T, Feldman C and Stone PH (1993) Relation of vessel wall shear stress to atherosclerosis progression in human coronary arteries. *Arterioscler Thromb.* **13(2)**:310-5.

Gloekler S, Seiler C (2007) Natural Bypasses Can Save Lives. *Circulation* **116**:e340-e341

Guha B, Majumder AAS, Chowdhury MNA, Hossain MM, Mandal AK (2012) Clinical Outcome and Echocardiographic Evaluation of Inferior Myocardial Infarction with Right Ventricular Involvement *Cardiovascular Journal* **4(2)**:132-138

Habib GB, Heibig J, Forman SA, Brown BG, Roberts R, Terrin ML, Bolli R (1991) Influence of coronary collateral vessels on myocardial infarct size in humans: Results of phase I Thrombolysis in Myocardial Infarction (TIMI) Trial: The TIMI Investigators. *Circulation* **83**: 739-746

Hamdan A, Asbach P, Wellnhofer E, Klein C, Gebker R, Kelle S, Kilian H, Huppertz A, Fleck E (2011) A Prospective Study for Comparison of MR and CT Imaging for Detection of Coronary Artery Stenosis. *J Am Coll Cardiol Img* **4**:50–61

Heaps CL, Parker JL (2011) Effects of exercise training on coronary collateralization and control of collateral resistance. *J Appl Physiol* **111(2)**: 587–598,

Hirai T, Fujita M, Nakajima H, Asanoi H, Yamanishi K, Ohno A, Sasayama S (1989) Importance of collateral circulation for prevention of left ventricular aneurysm formation in acute myocardial infarction. *Circulation* **79**:791-796

Hsu JT, Tamai H, Kyo E, Tsuji T, Watanabe S (2009) Traditional antegrade approach versus combined antegrade and retrograde approach in the percutaneous treatment of coronary chronic total occlusions. *Catheter Cardiovasc Interv* **74**:555-63.

Husanović A, Šišić F, Dilberović F, Ovćina F (2005) Collateral circulation of the human heart. *Bosnia Journal of basic Medical Sciences* **5(2)**: 87-91

Ilia R, Carmel S, Cafri C, Gueron M (1998) Coronary collaterals in patients with normal and impaired left ventricular systolic function. *Int J Cardiol* **63**:151–3.

Kattan J, Dettman RW, Bristow J (2004) Formation and remodeling of the coronary vascular bed in the embryonic avian heart. *Dev Dyn* **230**:34–43.

Kalpana RA (2003) A study on principal branches of coronary arteries in humans. *J Anat Soc India* **52(2)**: 137-140.

Kaul S (2008) Myocardial Contrast Echocardiography: A 25-Year Retrospective. *Circulation* **118**:291-308

Kahn JK, Hartzler GO (1990) Retrograde coronary angioplasty of isolated arterial segments through saphenous vein bypass grafts. *Cathet Cardiovasc Diagn* **20**:88–93

Khoo V, Shen L, Zhao L, Khoo V, Loo G, Richards AM, Yeo TC, Lee CH (2014) Determination of the severity of underlying lesions in acute myocardial infarction on the basis of collateral vessel development *Coron Artery Dis* **25**:493–497

Kilic C, Kirici Y (2007) Third branch derived from left coronary artery: the medial artery. *Gulhane tip Dergisi* **49**: 232–235

Killip T, Fisher LD, Mock MB (1981) The National Heart, Lung, and Blood Institute Coronary Artery Surgery Study (CASS) *Circulation* **63 (supplement 1)**: I-1-81

Kirpalani A, Park H, Butany J, Johnston KW, Ojha M (1999) Velocity and wall shear stress patterns in the human right coronary artery. *J Biomech Eng* **121(4)**: 370-375

Koerselman J, van der Graaf Y, de Jaegere PP, Grobbee DE (2003) Coronary collaterals: An important and underexposed aspect of coronary artery disease. *Circulation* **107**:2507–2511.

Koşar P, Ergun E, Öztürk C, Koşar U (2009) Anatomic variations and anomalies of the coronary arteries: 64-slice CT angiographic appearance. *Diagn Interv Radiol* **15**: 275–283

Kurjia HZ, Chaudhry MS, Olson TR (1986) Coronary Artery Variation in a Native Iraqi Population. *Cathet Cardiovasc Diagn* **12**: 386-390

Ladwiniec A and Hoye A (2013) Coronary Collaterals: A Little Give and Take, and a Few Unanswered Questions. *J Clin Exp Cardiolog* **4**:4

Levin DC, Kauff M, Baltaxe HA (1973) Coronary collateral circulation. *The American Journal of Roentgenology. Radium Therapy and Nuclear Medicine* **119(3)**: 463-473

Levin DC (1974) Pathways and functional significance of the coronary collateral circulation. *Circulation* **50**:831–837.

Loukas M, Bilinsky S, Bilinsky E, Petru M and Anderson RH (2009a) The Clinical Anatomy of the Coronary Collateral Circulation. *Clin Anat* **22**: 146–160.

Loukas M, Groat C, Khangura R, Owens DG and Anderson RH (2009b) The Normal and Abnormal Anatomy of the Coronary Arteries. *Clin Anat* **22**: 114–128.

Lujinović A, Ovcina F, Voljevica A, Hasanović A (2005) Branching of main trunk of left coronary artery and importance of her diagonal branch in cases of coronary insufficiency. *Bosn J Basic Med Sci.* **5(3)**: 69-73.

Maas AHEM, Appelman YEA (2010) Gender differences in coronary heart disease. *Neth Heart J* **18**: 598-603

Major RA (1932) Raymond Vieussens and His Treatise on the Heart. *Annals of Medical History* **4(2):** 147-154

Matsunaga T, Warltier DC, Weihrauch DW, Moniz M, Tessmer J, Chilian WM (2000) Ischemia-Induced Coronary Collateral Growth Is Dependent on Vascular Endothelial Growth Factor and Nitric Oxide. *Circulation* **102**:3098-3103

May AM (1960). Surgical anatomy of the coronary arteries. *Dis Chest* **38**:645–657

Mbewu A (2009) The burden of cardiovascular disease in sub-Saharan Africa. *SA Heart Journal* **6(1)**:1-9

Mian FA, Malik SN, Ismail M, Khan IS, Kachlu AR, Rehman M, Hussain J, Ahmad I (2011) Coronary Artery Dominance: What pattern exists in Pakistani Population? *Ann Pak Inst Med Sci* **7(1)**: 3-5

Mills JD, Fischer D, Villanueva FS (2000) Coronary collateral development during chronic ischemia: serial assessment using harmonic myocardial contrast echocardiography. *J Am Coll Cardiol* **36(2)**:618-24

Meier P, Gloekler S, Zbinden R, Beckh S, de Marchi SF, Zbinden S, Wustmann K, Billinger M, Vogel R, Cook S, Wenaweser P, Togni M, Windecker S, Meier B, Seiler C. (2007) Beneficial effect of recruitable collaterals: A 10-year follow-up study in patients with stable coronary artery disease undergoing quantitative collateral measurements. *Circulation* **116**: 975–983.

Meier P, Indermuehle A, Pitt B, Traupe T, de Marchi SF, Crake1 T, Knapp G, Lansky AJ, Seiler C. (2012) Coronary collaterals and risk for restenosis after percutaneous coronary intervention: a meta-analysis. *BMC Medicine* **10**: 62

Meier P, Schirmer SH, Lansky AJ, Timmis A, Pitt B and Seiler C (2013) The collateral circulation of the heart *BMC Medicine*, **11**:143

Miyamoto S, Masatoshi Fujita M, Sasayama S (2000) Bidirectional function of coronary collateral channels in humans. *Int J Cardiol* **75**: 249–252

Mock MB, Ringqvist I, Fisher LD, Davis KB, Chaitman BR, Kouchoukos NT, Kaiser GC Alderman E, Ryan TJ, Russell RO, Mullin S, Fray D, Killip T (1982) Survival of medically treated patients in the coronary artery surgery study (CASS) registry. *Circulation* **66**:562-568

Muriago M, Sheppard MN, Ho SY, Anderson RH. (1997) Location of the Coronary Arterial Orifices in the Normal Heart. *Clin Anat* **10**: 297–302

Myers JG, Moore JA, Ojha M, Johnston KW, Ethier CR (2001) Factors Influencing Blood Flow Patterns in the Human Right Coronary Artery *Ann Biomed Eng* **29**:109–120.

Nakae I, Fujita M, Miwa K, Hasegawa K, Kihara Y, Nohara R, Miyamoto S, Ueda K, Tamaki S, Sasayama S (2000) Age-dependent impairment of coronary collateral development in humans *Heart Vessels* **15**:176–180

Nerantzis CE, Papaciiristos JC, Gribizi JF, Voudris VA, Infantis GP, Koroxenidi G (1996) Functional Dominance of the Right Coronary Artery: Incidence in the Human Heart. *Clin Anat* **9**: 10-13

Ozawa N (2006) A new understanding of chronic total occlusion form a novel PCI technique that involves a retrograde approach to the right coronary artery via a septal branch and passing of the guidewire to a guiding catheter on the other side of the lesion. *Catheter Carsiovasc Interv* **68(6)**: 907-913

Park SJ, Park DW (2009) Percutaneous coronary intervention with stent implantation versus coronary artery bypass surgery for treatment of left main coronary artery disease. Is it time to change guidelines? *Circ Cardiovasc Interv* **2**: 59–68.

Paulin S (1967) Interarterial Coronary Anastomoses in Relation to Arterial Obstruction Demonstrated in Coronary Arteriography. *Investigative Radiology* **2(2)**:147-169

Piek JJ, Van Liebergen RA, Koch KT, Peters RJG, David GK (1997) Clinical, Angiographic and Hemodynamic Predictors of Recruitable Collateral Flow Assessed During Balloon Angioplasty Coronary Occlusion. *JACC* **29(2)**:275–82

Pohl T, Seiler C, Billinger M, Herren E, Wustmann K, Mehta H, Windecker S, Eberli FR, Meier B. (2001) Frequency distribution of collateral flow and factors influencing collateral channel development. Functional collateral channel measurement in 450 patients with coronary artery disease. *J Am Coll Cardiol* **38**:1872–1878.

Proudfit WJ, Bruschke AV, MacMillan JP, Williams GW, Sones FM (1983) Fifteen year survival study of patients with obstructive coronary artery disease. *Circulation* **68**:986-997

Raphael MJ, Hawtin DR and Allwork SP (1980) The angiographic anatomy of the coronary arteries. *Br J Surg* **67**: 181-187.

Rathore S, Matsuo H, Terashima M, Kinoshita Y, Kimura M, Tsuchikane E, Nasu K, Ehara M, Asakura Y, Katoh O, Suzuki T (2009) Procedural and In-Hospital Outcomes After Percutaneous Coronary Intervention for Chronic Total Occlusions of Coronary Arteries 2002 to 2008. *J Am Coll Cardiol Intv* **2**:489 –97

Reddy KS and Yusuf S (1998) Emerging Epidemic of Cardiovascular Disease in Developing Countries. *Circulation* **97**:596-601

Reig J, Petit M (2004) Main Trunk of the Left Coronary Artery: Anatomic Study of the Parameters of Clinical Interest. *Clin Anat* **17**: 6–13.

Rentrop KP, Cohen M, Blanke H, Phillips RA (1985) Changes in collateral filling after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol* **5** : 587–592.

Rockstroh J, Brown BG (2002) Coronary collateral size, flow capacity, and growth: Estimates from the angiogram in patients with obstructive coronary disease. *Circulation* **105**:168–173.

Ross R (1981) Atherosclerosis: a problem of the biology of arterial wall cells and their interactions with blood components. *Arteriosclerosis* **1**:293–311

Saleh AU, Shah AA, Ali SS, Shah ST (2013) Age and Gender Distribution in Patients with Acute ST Elevation Myocardial Infarction; A Survey in a Tertiary Care Government Hospital-NICVD, Karachi Pakistan. *The Internet Journal of Cardiology* 11(2)

Saltissi S,Webb-Peploe MM, Coltar DJ (1979) Effect of variation in coronary artery anatomy on distribution of stenotic lesions. *British Heart Journal* **42**: 186-191.

Sasayama S and Fujita M (1992) Recent insights into coronary collateral circulation. *Circulation* **85**:1197-1204

Scanlon PJ, Faxon DP (1999) ACC/AHA Guidelines for Coronary Angiography. *JACC* **33(6)**: 1756-1824

Schaper W (2009) Collateral circulation- Past and present *Basic Res Cardiol* **104**:5–21
Schenck-Gustafsson K (1996) Risk factors for cardiovascular disease in women:assessment and management *Eur Heart J* **17** (Suppl D): 2-8

Scher AM (2000) Absence of atherosclerosis in human intramyocardial coronary arteries: a neglected phenomenon. *Atherosclerosis* **149(1)**:1-3.

Schwartz H, Leiboff RL, Katz RJ, Wasserman AG, Bren GB, Varghese PJ, Ross AM (1985) Arteriographic predictors of spontaneous improvement in left ventricular function after myocardial infarction. *Circulation* **71**:466-472

Seiler C, Fleisch M, Garachemani A, Meier B (1998) Coronary Collateral Quantitation in Patients With Coronary Artery Disease Using Intravascular Flow Velocity or Pressure Measurements. *JACC* **32(5)**:1272–9

Seiler C, Billinger M, Fleisch M, Meier B (2001) Washout collaterometry: a new method of assessing collaterals using angiographic contrast clearance during coronary occlusion. *Heart* **186**: 540-546

Seiler C (2003) The human coronary collateral circulation. *Heart* **89**: 1352-1357

Senti S, Fleisch M, Billinger M, Meier B, Seiler C (1998) Long-term physical exercise and quantitatively assessed human coronary collateral circulation. *J Am Coll Cardiol* **32**: 49-56.

Shah PB (2011) Management of Coronary Chronic Total Occlusion. *Circulation* **123**:1780-1784

Sheehan F, Braunwald E, Canner P, Dodge HT, Gore J, Natt PV, Passamani ER, Williams DO, Zaret B (1987) The effect of intravenous thrombolytic therapy on left ventricular function: A report on tissue-type plasminogen activator and streptokinase from the Thrombolysis in Myocardial Infarction (TIMI Phase I) trial. *Circulation* **75**:817-829

Sun Z, Shen Y, Lu L, Zhang R, Pu L, Zhang Q, Yang Z, Hu J, Chen Q, Shen W (2013) Clinical and angiographic features associated with coronary collateralization in stable angina patients with chronic total occlusion. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)* **14(8)**:705-712

Surmely JF, Katoh O, Tsuchikane E, Nasu K, Suzuki T (2007) Coronary septal collaterals as an access for the retrograde approach in the percutaneous treatment of coronary chronic total occlusions. *Catheter Cardiovasc Interv* **69**:826-832

Tatli E, Altun A, Büyüklü M, Barotçu A (2007) Coronary collateral vessel development after acute myocardial infarction. *Exp Clin Cardiol* **12(2)**:97-99.

Traupe T, Gloekler S, de Marchi SF, Werner GS, Seiler C (2010) Assessment of the Human Coronary Collateral Circulation. *Circulation* **122**:1210-1220

Trappe HJ, Lichtlen PR, Klein H, Wenzlaff P, Hartwig CA (1989) Natural history of single vessel disease. Risk of sudden coronary death in relation to coronary anatomy and arrhythmia profile. *Eur Heart J* **10**: 514-524

Turgut O, Yilmaz MB, Yalta K, Tandogan I, Yilmaz A. (2009) Prognostic relevance of coronary collateral circulation: Clinical and epidemiological implications. *Int J Cardiol* **137(3)**:300-301

Valenti R, Migliorini A, Signorini U, Vergara R, Parodi G, Carrabba N, Cerisano G, Antoniucci D (2008) Impact of complete revascularization with percutaneous coronary intervention on survival in patients with at least one chronic total occlusion *Eur Heart J* **29**: 2336–2342

van der Hoeven NW, Teunissen PF, Werner GS, Delewi R, Schirmer SH, Traupe T, van der Laan AM, Tijssen JG, Piek JJ, Seiler C, van Royen N (2013) Clinical parameters associated with collateral development in patients with chronic total coronary occlusion. *Heart* **99**(15):1100-1105

van Royen N, Piek JJ, Buschmann I, Hoefer I, Voskuil M, Schaper W (2001) Stimulation of arteriogenesis; a new concept for the treatment of arterial occlusive disease *Cardiovasc Res* **49**: 543–553

Vanker EA, Ajayi NO, Lazarus L, Satyapal KS (2014) The intramyocardial left anterior descending artery: Prevalence and surgical considerations in coronary artery bypass grafting. *S Afr J Surg* **52(1)**:18-21

Vilallonga JR (2003) Anatomical variations of the coronary arteries: The most frequent variations. *Eur J Anat* 7 Suppl. **1**: 29-41

Vogel R, Zbinden R, Indermùhle A, Windecker S, Meier B, Seiler C (2006) Collateral-flow measurements in humans by myocardial contrast echocardiography: validation of coronary pressure-derived collateral-flow assessment *Eur Heart J* **27**:157–165

Wackers J, Terrin ML, Kayden DS, Knatterud G, Forman S, Braunwald E, Zaret BL, and the TIMI investigators (1989) Quantitative radionuclide assessment of regional ventricular function after thrombolytic therapy for acute myocardial infarction: Results of Phase I Thrombolysis in Myocardial Infarction (TIMI) trial. *J Am Coll Cardiol* **13**:998-1005

Wainwright RJ, Maisey MN, Edwards AC, Sowton E. 1980. Functional significance of coronary collateral circulation during dynamic exercise evaluated by thallium-201 myocardial scintigraphy. *Br Heart J* **43**:47–55.

Werner GS, Ferrari M, Heinke S, Kuethe F, Surber R, Richartz BM, Figulla HR (2003) Angiographic Assessment of Collateral Connections in Comparison With Invasively Determined Collateral Function in Chronic Coronary Occlusions. *Circulation* **107**:1972-1977

Wustmann K, Zbinden S, Windecker S, Meier B, Seiler C (2003) Is there functional collateral flow during vascular occlusion in angiographically normal coronary arteries? *Circulation* **107**:2213–2220.

Zbinden R, Zbinden S, Billinger M, Windecker S, Meier B, Seiler C (2005) Influence of diabetes mellitus on coronary collateral flow: an answer to an old controversy. *Heart* **91**:1289–1293

TEXTBOOKS

Allen HD, Driscoll DJ, Shaddy RE, Feltes TF (2000) Moss and Adam's Heart Disease in Infants, Children and Adolescents 6th Ed. Lippincott Williams & Wilkins

Bonow *et al.* (2011) Braunwald's Heart Disease. A Textbook of cardiovascular Medicine, 9th ed. Saunders

Drake R, Wayne Vogl A, Mitchell AWM (2009). Gray's Anatomy for Students, 2nd Edition, Churchill Livingstone

Gilroy A, MacPherson B, Ross L (2008). Atlas of Anatomy. Thieme Medical Publishers, Inc. page 88

Moore KL, Dalley AF, Agur AMR (2010). Clinically Oriented Anatomy. 6th Ed Lippincott Williams & Wilkins

Netter FH (2003) Atlas of Human Anatomy. 4th Ed. Saunders Elsevier

Sinnatamby CS (2006). Last's anatomy: regional and applied. 11th Ed. Edinburgh: Churchill Livingstone.

Snell RS (2008) Clinical Anatomy by Regions. 8th Ed. Lippincott Williams and Wilkins

Standring S, Ellis H, Healy JC, Johnson D, Williams A *et al*. (2008) Gray's Anatomy. 40th Ed., Newyork, Elsevier Churchill Livinstone

Townsend CM, Beauchamp RD, Evers BM, Mattox LM (2004)**:** Sabiston Textbook of Surgery, 17th ed. Elsevier

Topol EJ, Califf RM, Isner J, Prsytowsky E, Swain J, Thomas J, Thompson P, Young JB, Nissen S (2002) Textbook of Cardiovascular Medicine. Lippincott Williams and Wilkins

Vlodaver Z, Neufeld HN, Edwards JE (1975). Coronary Arterial Variations in the Normal Heart and in Congenital Heart Disease. New York: Acoronary artery diseaseemic Press

APPENDICES

APPENDIX A

SAMPLE DISTRIBUTION

Statistics

		Sex	Branching	DoMinance	VesselDx
N	Valid	286	286	286	286
	Missing	0	0	0	0

FREQUENCY TABLE

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	62	21.7	21.7	21.7
	Male	224	78.3	78.3	100.0
	Total	286	100.0	100.0	

Branching

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Bifurcation	260	90.9	90.9	90.9
	Trifurcation	25	8.7	8.7	99.7
	Quadrifurcation	1	.3	.3	100.0
	Total	286	100.0	100.0	

DoMinance

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Co-dominance	10	3.5	3.5	3.5
	Left	39	13.6	13.6	17.1
	Right	237	82.9	82.9	100.0
	Total	286	100.0	100.0	

VesselDx

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Double	37	12.9	12.9	12.9
	Single	246	86.0	86.0	99.0
	Triple	3	1.0	1.0	100.0
	Total	286	100.0	100.0	

MEAN AGE

Descriptives

	Sex			Statistic	Std. Error
Age	Female	Mean		63.929	1.5206
		95% Confidence Interval for Mean	Lower Bound	60.881	
			Upper Bound	66.976	
		5% Trimmed Mean		63.746	
		Median		63.500	
		Variance		129.486	
		Std. Deviation		11.3792	
		Minimum		42.0	
		Maximum		93.0	
		Range		51.0	
		Interquartile Range		18.0	
		Skewness		.215	.319
		Kurtosis		-.337	.628
	Male	Mean		57.399	.6979
		95% Confidence Interval for Mean	Lower Bound	56.023	
			Upper Bound	58.775	
		5% Trimmed Mean		57.481	
		Median		57.000	
		Variance		101.323	
		Std. Deviation		10.0659	
		Minimum		29.0	
		Maximum		87.0	
		Range		58.0	
		Interquartile Range		13.0	
		Skewness		-.085	.169
		Kurtosis		.206	.336

ANOVA Table[a]

			Sum of Squares	df	Mean Square	F	Sig.
Age * Sex	Between Groups	(Combined)	1881.099	1	1881.099	17.542	.000
	Within Groups		28095.594	262	107.235		
	Total		29976.693	263			

a. The grouping variable Sex is a string, so the test for linearity cannot be computed.

APPENDIX B

GRADING OF THE CORONARY COLLATERALS

A. ANTERIOR INTERVENTRICULAR BRANCH

GradingoFcoll * Age categ

Crosstab

			Age categ		Total
			>60 yrs	≤ 60 yrs	
GradingoFcoll	Absent	Count	7	13	20
		% within GradingoFcoll	35.0%	65.0%	100.0%
		% within Age categ	22.6%	33.3%	28.6%
		% of Total	10.0%	18.6%	28.6%
	Poor	Count	3	7	10
		% within GradingoFcoll	30.0%	70.0%	100.0%
		% within Age categ	9.7%	17.9%	14.3%
		% of Total	4.3%	10.0%	14.3%
	Good	Count	11	12	23
		% within GradingoFcoll	47.8%	52.2%	100.0%
		% within Age categ	35.5%	30.8%	32.9%
		% of Total	15.7%	17.1%	32.9%
	Excellent	Count	10	7	17
		% within GradingoFcoll	58.8%	41.2%	100.0%
		% within Age categ	32.3%	17.9%	24.3%
		% of Total	14.3%	10.0%	24.3%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.099[a]	3	.377
Likelihood Ratio	3.133	3	.372
N of Valid Cases	70		
a. 1 cells (12.5%) have expected count less than 5. The minimum expected count is 4.43.			

GradingoFcoll * Sex

Crosstab					
			Sex		Total
			Female	Male	
GradingoFcoll	Absent	Count	5	18	23
		% within GradingoFcoll	21.7%	78.3%	100.0%
		% within Sex	31.3%	30.0%	30.3%
		% of Total	6.6%	23.7%	30.3%
	Poor	Count	1	9	10
		% within GradingoFcoll	10.0%	90.0%	100.0%
		% within Sex	6.3%	15.0%	13.2%
		% of Total	1.3%	11.8%	13.2%
	Good	Count	7	18	25
		% within GradingoFcoll	28.0%	72.0%	100.0%
		% within Sex	43.8%	30.0%	32.9%
		% of Total	9.2%	23.7%	32.9%
	Excellent	Count	3	15	18
		% within GradingoFcoll	16.7%	83.3%	100.0%
		% within Sex	18.8%	25.0%	23.7%
		% of Total	3.9%	19.7%	23.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.676[a]	3	.642
Likelihood Ratio	1.773	3	.621
N of Valid Cases	76		

GradingoFcoll * Dominance

Crosstab

			Dominance			Total
			Co-dominance	Left	Right	
GradingoFcoll	Absent	Count	1	3	19	23
		% within GradingoFcoll	4.3%	13.0%	82.6%	100.0%
		% within Dominance	33.3%	27.3%	30.6%	30.3%
		% of Total	1.3%	3.9%	25.0%	30.3%
	Poor	Count	2	2	6	10
		% within GradingoFcoll	20.0%	20.0%	60.0%	100.0%
		% within Dominance	66.7%	18.2%	9.7%	13.2%
		% of Total	2.6%	2.6%	7.9%	13.2%
	Good	Count	0	5	20	25
		% within GradingoFcoll	0.0%	20.0%	80.0%	100.0%
		% within Dominance	0.0%	45.5%	32.3%	32.9%
		% of Total	0.0%	6.6%	26.3%	32.9%
	Excellent	Count	0	1	17	18
		% within GradingoFcoll	0.0%	5.6%	94.4%	100.0%
		% within Dominance	0.0%	9.1%	27.4%	23.7%
		% of Total	0.0%	1.3%	22.4%	23.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.942[a]	6	.090
Likelihood Ratio	9.659	6	.140
N of Valid Cases	76		

a. 8 cells (66.7%) have expected count less than 5. The minimum expected count is .39.

GradingoFcoll * lesionlocation

Crosstab

			lesionlocation			Total
			Proximal	Middle	Distal	
GradingoFcoll	Absent	Count	13	10	0	23
		% within GradingoFcoll	56.5%	43.5%	0.0%	100.0%
		% within lesionlocation	27.1%	38.5%	0.0%	30.3%
		% of Total	17.1%	13.2%	0.0%	30.3%
	Poor	Count	5	4	1	10
		% within GradingoFcoll	50.0%	40.0%	10.0%	100.0%
		% within lesionlocation	10.4%	15.4%	50.0%	13.2%
		% of Total	6.6%	5.3%	1.3%	13.2%
	Good	Count	18	7	0	25
		% within GradingoFcoll	72.0%	28.0%	0.0%	100.0%
		% within lesionlocation	37.5%	26.9%	0.0%	32.9%
		% of Total	23.7%	9.2%	0.0%	32.9%
	Excellent	Count	12	5	1	18
		% within GradingoFcoll	66.7%	27.8%	5.6%	100.0%
		% within lesionlocation	25.0%	19.2%	50.0%	23.7%
		% of Total	15.8%	6.6%	1.3%	23.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.865[a]	6	.438
Likelihood Ratio	6.114	6	.411
N of Valid Cases	76		

a. 5 cells (41.7%) have expected count less than 5. The minimum expected count is .26.

B. CIRCUMFLEX BRANCH

GradingoFcoll * Age category

Crosstab

			Age category		Total
			>60 yrs	≤ 60 yrs	
GradingoFcoll	Absent	Count	18	9	27
		% within GradingoFcoll	66.7%	33.3%	100.0%
		% within Age category	47.4%	22.5%	34.6%
		% of Total	23.1%	11.5%	34.6%
	Poor	Count	7	9	16
		% within GradingoFcoll	43.8%	56.3%	100.0%
		% within Age category	18.4%	22.5%	20.5%
		% of Total	9.0%	11.5%	20.5%
	Good	Count	9	12	21
		% within GradingoFcoll	42.9%	57.1%	100.0%
		% within Age category	23.7%	30.0%	26.9%
		% of Total	11.5%	15.4%	26.9%
	Excellent	Count	4	10	14
		% within GradingoFcoll	28.6%	71.4%	100.0%
		% within Age category	10.5%	25.0%	17.9%
		% of Total	5.1%	12.8%	17.9%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.203[a]	3	.102
Likelihood Ratio	6.344	3	.096
N of Valid Cases	78		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 6.82.

GradingoFcoll * Sex

Crosstab

			Sex		Total
			Female	Male	
GradingoFcoll	Absent	Count	10	19	29
		% within GradingoFcoll	34.5%	65.5%	100.0%
		% within Sex	40.0%	30.6%	33.3%
		% of Total	11.5%	21.8%	33.3%
	Poor	Count	5	12	17
		% within GradingoFcoll	29.4%	70.6%	100.0%
		% within Sex	20.0%	19.4%	19.5%
		% of Total	5.7%	13.8%	19.5%
	Good	Count	9	17	26
		% within GradingoFcoll	34.6%	65.4%	100.0%
		% within Sex	36.0%	27.4%	29.9%
		% of Total	10.3%	19.5%	29.9%
	Excellent	Count	1	14	15
		% within GradingoFcoll	6.7%	93.3%	100.0%
		% within Sex	4.0%	22.6%	17.2%
		% of Total	1.1%	16.1%	17.2%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.478[a]	3	.214
Likelihood Ratio	5.510	3	.138
N of Valid Cases	87		

a. 2 cells (25.0%) have expected count less than 5. The minimum expected count is 4.31.

GradingoFcoll * DoMinance

Crosstab

			DoMinance			Total
			Co-dominance	Left	Right	
GradingoFcoll	Absent	Count	0	2	27	29
		% within GradingoFcoll	0.0%	6.9%	93.1%	100.0%
		% within DoMinance	0.0%	10.5%	40.9%	33.3%
		% of Total	0.0%	2.3%	31.0%	33.3%
	Poor	Count	0	5	12	17
		% within GradingoFcoll	0.0%	29.4%	70.6%	100.0%
		% within DoMinance	0.0%	26.3%	18.2%	19.5%
		% of Total	0.0%	5.7%	13.8%	19.5%
	Good	Count	2	9	15	26
		% within GradingoFcoll	7.7%	34.6%	57.7%	100.0%
		% within DoMinance	100.0%	47.4%	22.7%	29.9%
		% of Total	2.3%	10.3%	17.2%	29.9%
	Excellent	Count	0	3	12	15
		% within GradingoFcoll	0.0%	20.0%	80.0%	100.0%
		% within DoMinance	0.0%	15.8%	18.2%	17.2%
		% of Total	0.0%	3.4%	13.8%	17.2%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	12.434[a]	6	.053
Likelihood Ratio	13.351	6	.038
N of Valid Cases	87		

a. 6 cells (50.0%) have expected count less than 5. The minimum expected count is .34.

GradingoFcoll * lesionlocation

Crosstab

			lesionlocation			Total
			Proximal	Middle	Distal	
GradingoFcoll	Absent	Count	18	8	3	29
		% within GradingoFcoll	62.1%	27.6%	10.3%	100.0%
		% within lesionlocation	45.0%	26.7%	17.6%	33.3%
		% of Total	20.7%	9.2%	3.4%	33.3%
	Poor	Count	6	8	3	17
		% within GradingoFcoll	35.3%	47.1%	17.6%	100.0%
		% within lesionlocation	15.0%	26.7%	17.6%	19.5%
		% of Total	6.9%	9.2%	3.4%	19.5%
	Good	Count	10	10	6	26
		% within GradingoFcoll	38.5%	38.5%	23.1%	100.0%
		% within lesionlocation	25.0%	33.3%	35.3%	29.9%
		% of Total	11.5%	11.5%	6.9%	29.9%
	Excellent	Count	6	4	5	15
		% within GradingoFcoll	40.0%	26.7%	33.3%	100.0%
		% within lesionlocation	15.0%	13.3%	29.4%	17.2%
		% of Total	6.9%	4.6%	5.7%	17.2%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.969[a]	6	.324
Likelihood Ratio	6.832	6	.337
N of Valid Cases	87		

a. 2 cells (16.7%) have expected count less than 5. The minimum expected count is 2.93.

C. RIGHT CORONARY ARTERY

GradingoFcoll * Age cat Crosstabulation					
			Age cat		Total
			>60 yrs	≤ 60 yrs	
GradingoFcoll	Absent	Count	15	16	31
		% within GradingoFcoll	48.4%	51.6%	100.0%
		% within Age cat	22.1%	18.0%	19.7%
		% of Total	9.6%	10.2%	19.7%
	Poor	Count	6	11	17
		% within GradingoFcoll	35.3%	64.7%	100.0%
		% within Age cat	8.8%	12.4%	10.8%
		% of Total	3.8%	7.0%	10.8%
	Good	Count	32	27	59
		% within GradingoFcoll	54.2%	45.8%	100.0%
		% within Age cat	47.1%	30.3%	37.6%
		% of Total	20.4%	17.2%	37.6%
	Excellent	Count	15	35	50
		% within GradingoFcoll	30.0%	70.0%	100.0%
		% within Age cat	22.1%	39.3%	31.8%
		% of Total	9.6%	22.3%	31.8%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	7.247[a]	3	.064
Likelihood Ratio	7.360	3	.061
N of Valid Cases	157		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.36.

GradingoFcoll * lesionlocation

Crosstab

			lesionlocation			Total
			Proximal	Middle	Distal	
GradingoFcoll	Absent	Count	15	10	7	32
		% within GradingoFcoll	46.9%	31.3%	21.9%	100.0%
		% within lesionlocation	21.7%	15.4%	21.9%	19.3%
		% of Total	9.0%	6.0%	4.2%	19.3%
	Poor	Count	4	11	3	18
		% within GradingoFcoll	22.2%	61.1%	16.7%	100.0%
		% within lesionlocation	5.8%	16.9%	9.4%	10.8%
		% of Total	2.4%	6.6%	1.8%	10.8%
	Good	Count	20	28	17	65
		% within GradingoFcoll	30.8%	43.1%	26.2%	100.0%
		% within lesionlocation	29.0%	43.1%	53.1%	39.2%
		% of Total	12.0%	16.9%	10.2%	39.2%
	Excellent	Count	30	16	5	51
		% within GradingoFcoll	58.8%	31.4%	9.8%	100.0%
		% within lesionlocation	43.5%	24.6%	15.6%	30.7%
		% of Total	18.1%	9.6%	3.0%	30.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	15.230[a]	6	.019
Likelihood Ratio	15.441	6	.017
N of Valid Cases	166		

a. 1 cells (8.3%) have expected count less than 5. The minimum expected count is 3.47.

GradingoFcoll * Sex

Crosstab

			Sex		Total
			Female	Male	
GradingoFcoll	Absent	Count	7	25	32
		% within GradingoFcoll	21.9%	78.1%	100.0%
		% within Sex	22.6%	18.5%	19.3%
		% of Total	4.2%	15.1%	19.3%
	Poor	Count	4	14	18
		% within GradingoFcoll	22.2%	77.8%	100.0%
		% within Sex	12.9%	10.4%	10.8%
		% of Total	2.4%	8.4%	10.8%
	Good	Count	15	50	65
		% within GradingoFcoll	23.1%	76.9%	100.0%
		% within Sex	48.4%	37.0%	39.2%
		% of Total	9.0%	30.1%	39.2%
	Excellent	Count	5	46	51
		% within GradingoFcoll	9.8%	90.2%	100.0%
		% within Sex	16.1%	34.1%	30.7%
		% of Total	3.0%	27.7%	30.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.837[a]	3	.280
Likelihood Ratio	4.215	3	.239
N of Valid Cases	166		

a. 1 cells (12.5%) have expected count less than 5. The minimum expected count is 3.36.

GradingoFcoll * DoMinance

Crosstab

			DoMinance			Total
			Co-dominance	Left	Right	
GradingoFcoll	Absent	Count	2	10	20	32
		% within GradingoFcoll	6.3%	31.3%	62.5%	100.0%
		% within DoMinance	25.0%	50.0%	14.5%	19.3%
		% of Total	1.2%	6.0%	12.0%	19.3%
	Poor	Count	0	0	18	18
		% within GradingoFcoll	0.0%	0.0%	100.0%	100.0%
		% within DoMinance	0.0%	0.0%	13.0%	10.8%
		% of Total	0.0%	0.0%	10.8%	10.8%
	Good	Count	3	6	56	65
		% within GradingoFcoll	4.6%	9.2%	86.2%	100.0%
		% within DoMinance	37.5%	30.0%	40.6%	39.2%
		% of Total	1.8%	3.6%	33.7%	39.2%
	Excellent	Count	3	4	44	51
		% within GradingoFcoll	5.9%	7.8%	86.3%	100.0%
		% within DoMinance	37.5%	20.0%	31.9%	30.7%
		% of Total	1.8%	2.4%	26.5%	30.7%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	16.654[a]	6	.011
Likelihood Ratio	16.910	6	.010
N of Valid Cases	166		

a. 6 cells (50.0%) have expected count less than 5. The minimum expected count is .87.

APPENDIX C

STATISTICAL ANALYSIS IN PATIENTS WHO HAD LEFT VENTRICULOGRAPHY

Frequency Table

Sex

	Frequency	Percent	Valid Percent	Cumulative Percent
Female	25	25.8	25.8	25.8
Male	72	74.2	74.2	100.0
Total	97	100.0	100.0	

DoMinance

	Frequency	Percent	Valid Percent	Cumulative Percent
Co-dominance	3	3.1	3.1	3.1
Left	13	13.4	13.4	16.5
Right	81	83.5	83.5	100.0
Total	97	100.0	100.0	

lesionlocation

	Frequency	Percent	Valid Percent	Cumulative Percent
Proximal	44	45.4	45.4	45.4
Middle	37	38.1	38.1	83.5
Distal	16	16.5	16.5	100.0
Total	97	100.0	100.0	

GradingoFcoll

	Frequency	Percent	Valid Percent	Cumulative Percent
Absent	16	16.5	16.5	16.5
Poor	13	13.4	13.4	29.9
Good	35	36.1	36.1	66.0
Excellent	33	34.0	34.0	100.0
Total	97	100.0	100.0	

Oneway

Descriptives

EF

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Absent	16	50.388	17.6187	4.4047	40.999	59.776	19.4	74.3
Poor	13	47.000	12.0475	3.3414	39.720	54.280	29.4	66.3
Good	35	60.511	18.8730	3.1901	54.028	66.995	18.7	84.7
Excellent	33	69.961	13.8473	2.4105	65.051	74.871	29.7	88.4
Total	97	60.245	18.1421	1.8421	56.589	63.902	18.7	88.4

ANOVA

EF

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	6952.769	3	2317.590	8.746	.000
Within Groups	24644.412	93	264.994		
Total	31597.180	96			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: EF

	(I) GradingoFcoll	(J) GradingoFcoll	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tamhane	Absent	Poor	3.3875	5.5287	.991	-12.334	19.109
		Good	-10.1239	5.4386	.362	-25.402	5.154
		Excellent	-19.5731*	5.0211	.004	-33.948	-5.199
	Poor	Absent	-3.3875	5.5287	.991	-19.109	12.334
		Good	-13.5114*	4.6197	.036	-26.417	-.606
		Excellent	-22.9606*	4.1201	.000	-34.720	-11.201
	Good	Absent	10.1239	5.4386	.362	-5.154	25.402
		Poor	13.5114*	4.6197	.036	.606	26.417
		Excellent	-9.4492	3.9984	.121	-20.314	1.415
	Excellent	Absent	19.5731*	5.0211	.004	5.199	33.948
		Poor	22.9606*	4.1201	.000	11.201	34.720
		Good	9.4492	3.9984	.121	-1.415	20.314

*. The mean difference is significant at the 0.05 level.

Nonparametric Correlations

Correlations

			GradingoFcoll	EF
Spearman's rho	GradingoFcoll	Correlation Coefficient	1.000	.478**
		Sig. (2-tailed)	.	.000
		N	97	97
	EF	Correlation Coefficient	.478**	1.000
		Sig. (2-tailed)	.000	.
		N	97	97

**. Correlation is significant at the 0.01 level (2-tailed).

APPENDIX D

A. RAW DATA IN PATIENTS WITH ANTERIOR INTERVENTRICULAR

BRANCH OBSTRUCTION

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF (%)
1		F	B	R	12	0	
2	53	M	B	L	12	0	
3		F	B	L	15	1,2	
4	49	M	B	R	16	1	
5	45	M	B	R	15	2	
6	77	F	B	R	12	2	
7	37	M	T	R	12	2	
8	53	M	B	L	12	1	
9	48	M	B	R	14	3	
10	51	M	B	co	12	1	
11	55	M	B	R	14	1	
12	51	M	B	Co	12	1	
13	33	M	B	R	12	0	
14	64	F	B	R	12	0	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF (%)
15	54	M	B	R	13	0	
16		M	B	R	12	0	
17	77	F	B	R	12	2	43.6
18	56	M	B	L	15	0	19.4
19	31	M	B	R	13	1	
20	45	M	B	R	13	2	31
21	61	M	B	R	12	1	29.4
22	59	F	B	R	12	3	85.3
23	32	M	B	R	12	2	
24	54	M	B	R	12	0	
25	52	F	B	R	12	0	
26	63	M	B	R	12	3	67.2
27	70	M	B	R	13	3	
28	44	M	B	R	12	2	
29	51	M	B	Co	13	0	
30	56	M	B	R	12	3	35
31	52	M	B	L	12	2	
32		M	B	R	12	2	
33		M	B	L	12	3	29.9
34	37	M	B	L	12	1	
35	73	M	B	R	13	3	81
36	61	M	T	R	15	2	
37	55	M	B	R	13	2	
38		F	T	R	13	0	63.3
39	87	M	B	R	12	2	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF (%)
40	66	M	B	L	12	2	82.8
41	49	M	B	R	15	2	
42	62	M	B	L	13	2	
43	65	F	B	R	13	1	
44	68	M	B	R	15	0	
45	38	M	B	R	12	3	
46	67	F	B	R	13	3	85.9
47	66	M	T	R	12	3	
48	45	M	T	R	12	3	
49	65	M	B	L	15	2	
50	65	F	B	R	12	3	
51	78	F	B	R	12	2	
52	58	M	B	R	12	3	72.4
53	41	M	B	R	13	0	
54	53	M	B	R	13	2	
55	59	M	B	R	13	0	
56	45	M	B	R	13	3	
57	56	M	B	R	13	0	
58	70	M	B	R	13	0	
59	65	M	B	R	12	0	
60	47	M	B	R	12	2	72.7
61	67	M	B	R	12	3	64.2
62	60	F	B	R	12	2	34.1
63	68	M	B	R	13	0	
64	61	M	B	R	16	1	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF (%)
65	61	M	T	R	12	2	48
66	62	M	B	R	13	3	
67	61	M	B	R	15	0	74.3
68	52	M	B	R	13	0	26.7
69	69	F	B	R	16	2	84.3
70	62	F	B	R	13	2	44.7
71	68	M	B	L	12	0	
72	55	M	B	R	12	0	
73	48	M	B	R	13	2	
74	74	M	B	R	12	2,3	
75	50	F	B	R	13	0	
76	71	M	B	R	12	3	86.5

B. RAW DATA IN PATIENTS WITH CIRCUMFLEX BRANCH OBSTRUCTION

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
1	59	F	T	R	19a	2	72.8
2	49	M	B	L	19	2	18.7
3	57	M	B	R	19	1	66.3
4	86	F	B	R	18	2	84.7
5	71	M	B	R	18	0	
6	53	M	T	R	18	1	61.7
7		M	B	R	23	1	
8	54	F	B	L	21	2	79.8
9	60	M	T	R	18	3	
10	62	M	B	L	19a	1	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
11	55	M	B	R	18	0	
12	83	F	B	L	18	2	
13	49	M	T	R	18	2	
14	51	M	B	R	19a	3	
15	43	F	B	L	19	1	
16	71	M	B	R	18	3	74.7
17	56	M	T	R	19a	3	
18	83	M	B	R	19	0	
19	59	M	B	R	19	0	47.8
20	64	F	B	R	18	0	
21	52	M	B	R	19	0	57.5
22	45	M	T	R	18	0	61.7
23	68	M	B	R	18	0	
24	63	F	B	R	20	0	
25	64	M	B	R	18	0	
26	55	M	B	R	19	3	64.2
27	62	F	B	R	18	0	55.8
28		F	B	R	19a	0	
29	52	F	B	R	18	2	54.3
30		M	B	R	18	3	
31	51	M	B	Co	21	2	64.4
32	52	F	B	R	18	0	
33	48	M	B	R	19a	3	73.4
34	50	F	T	R	20	3	68.1
35	63	M	B	R	19	0	
36	72	F	B	R	19	0	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
37	56	M	B	R	19	1	35
38	59	M	B	R	20	0	
39	70	M	B	R	20	3	
40		M	B	L	19	2	29.9
41	53	M	B	L	19	2	54
42	54	M	B	L	19a	3	
43	63	M	B	R	19	0	
44	50	M	B	R	18	0	57.9
45	75	F	B	L	18	0	
46		M	B	L	18	2	
47	61	M	B	R	20	0	30.9
48	61	M	B	L	23	2	
49	63	F	B	co	20	2	74.9
50		M	B	R	21	2	34.1
51	67	M	B	L	19	1	45.5
52	78	M	B	R	19a	2	60.9
53	65	F	B	R	18	1	58.8
54	62	M	B	L	19	3	
55	65	F	B	R	20	2	
56	59	M	B	L	23	2	
57	63	M	B	R	19	2	
58	73	M	B	R	21	1	
59	69	M	B	R	20	2	
60	46	F	B	L	23	2	
61	62	F	B	R	23	0	27.9
62	51	M	B	R	18	2	79.6

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
63	52	F	B	L	23	1	44.3
64	51	M	B	R	18	0	
65	71	F	B	R	18	0	66.6
66	49	F	B	R	19	1	
67	43	M	B	R	19	3	
68	70	M	B	R	18	0	
69	45	M	T	R	20	1	61.2
70	50	M	B	R	19a	0	65.4
71	61	M	B	R	19	3	
72	50	M	B	R	18	3	
73	57	M	B	R	18	1	
74	65	M	B	R	19	0	29.3
75		M	B	R	18	0	
76	74	M	B	L	19	0	
77	61	M	B	R	21	1	
78	59	M	B	L	19a	3	29.7
79	61	M	T	R	21	2	
80	62	M	B	R	21	1	
81	83	F	B	R	18	1	
82	67	F	B	R	18	0	
83		M	B	R	19	2	67.9
84	53	M	B	L	20	1	
85		M	B	R	19	2	
86	57	F	B	R	18	2	
87	52	M	B	R	19a	2	

C. RAW DATA IN PATIENTS WITH RIGHT CORONARY ARTERY OBSTRUCTION

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
1	63	M	B	R	3	2	19.2
2	57	M	B	R	2	2	
3	73	M	B	R	2	3	71.5
4	58	M	Q	R	2	3	60.6
5	61	M	B	R	2	2	
6	66	M	B	R	1	2	63.1
7	77	F	B	R	2	2	
8		M	B	R	3	2	
9	76	F	B	R	5	2	
10	63	M	B	R	2	2	
11	42	M	B	R	3	2	
12	77	F	B	R	2	2	
13	65	F	B	R	3	2	
14	61	M	B	R	5	1	49.9
15	53	M	B	R	1	3	
16	44	M	B	R	2	1	
17	54	F	B	L	1	3	79.8
18	61	M	B	R	1	3	
19	56	M	B	R	1	3	
20		F	B	co	3	2	
21	61	M	B	R	2	2	
22	53	M	B	L	2	0	
23	56	M	B	co	1	0	
24	47	M	B	R	2	1	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
25	55	M	B	R	3	2	
26	59	M	B	R	1	2	
27	43	M	B	R	2	1	
28	46	M	B	R	1	0	
29		M	B	R	1	2	
30	54	F	B	R	2	2	
31	77	F	B	Co	2	3	
32	63	M	B	R	2	2	68.1
33	57	M	B	L	1	0	
34	48	M	T	R	2	3	
35	58	M	B	R	3	2	
36	52	M	B	R	2	2	
37	68	M	B	L	1	0	
38	41	M	B	R	1	3	
39	59	M	B	R	1	0	
40	50	M	B	L	1	0	
41	66	F	T	R	1	3	
42	48	M	B	R	2	2	
43	52	M	B	R	4	2	57.5
44	49	M	B	R	3	0	
45	80	M	B	R	2	0	
46	45	M	T	R	1	3	61.7
47	74	M	B	R	1	2	49.5
48	80	M	B	R	1	2	
49	52	M	T	R	2	2	
50	68	M	B	R	1	2	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
51	64	M	B	R	1	2	
52	55	M	B	R	2	1	64.2
53	53	M	B	R	2	2	
54	56	M	B	L	2	0	19.4
55	44	M	B	R	3	0	57.7
56	39	M	B	R	2	1	44.9
57	60	F	B	L	2	0	56.1
58	44	M	B	R	4	2	
59	67	M	B	R	2	2	48.4
60	51	M	B	Co	1	3	64.4
61	55	M	B	R	2	3	
62	63	M	B	R	2	3	67.2
63	61	F	B	R	1	3	84.4
64	48	M	B	R	2	3	73.4
65		M	T	L	1	2	
66	72	M	B	R	3	2	
67	50	F	T	R	2	2	68.1
68	44	M	B	R	2	3	
69	55	M	B	R	1	2	71.3
70	51	M	B	Co	1	3	
71	48	M	B	R	2	3	
72	73	F	B	R	1	0	
73	57	M	B	L	2	0	
74	56	M	B	R	1	1	35
75		M	B	R	2	0	
76	73	M	B	R	2	0	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
77	54	M	B	R	1	3	72.6
78	60	M	T	R	1	3	
79	60	M	B	R	2	3	55.7
80	62	M	B	Co	2	0	
81	37	M	B	L	2	2	
82	77	M	B	R	1	3	77.6
83	68	F	B	R	3	0	
84	58	M	B	R	1	3	54.4
85	53	F	B	R	2	3	76.3
86	47	M	B	R	3	3	59.3
87	66	M	B	R	3	3	
88	41	M	B	R	4	3	74.6
89	68	M	B	R	1	2	63.8
90	61	M	B	L	1	3	
91	63	M	B	R	1	3	
92	63	F	B	co	2	2	74.9
93	57	M	B	R	3	3	
94	55	M	B	R	1	0	
95	74	M	B	R	1	1	
96	45	M	B	R	1	2	
97	50	M	B	R	2	1	
98	51	M	T	L	1	0	68.7
99		M	B	R	4	1	34.1
100	61	F	B	R	1	2	76.2
101	57	F	B	R	1	2	38.8
102	69	M	B	R	2	2	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
103	49	M	B	R	1	3	
104	65	F	B	R	3	1	58.8
105	58	M	B	L	2	0	
106	62	M	B	L	1	2	
107	60	M	B	R	2	1	30.3
108	72	F	B	R	2	1	
109	65	F	B	R	4	0	
110	68	M	B	R	1	0	
111	38	M	B	R	2	3	
112	50	M	B	R	1	3	
113	73	M	B	R	1	2	
114	55	M	B	R	1	2	
115	93	F	B	R	1	0	
116	70	M	B	R	2	2	
117	57	M	B	R	1	3	74.2
118	49	M	B	R	1	0	
119	65	M	B	L	2	2	
120	62	F	B	R	4	0	27.9
121	66	M	B	R	3	2	70.2
122	55	M	B	R	1	0	
123	59	M	B	R	1	3	
124	62	M	B	L	1	0	58.4
125	63	M	B	R	2	2	
126	70	F	T	L	2	2	
127	65	M	B	R	2	3	78.9
128	67	F	B	R	2	0	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
129	66	M	B	R	2	1	43.3
130	59	M	B	R	1	3	
131		M	B	R	3	2	82.6
132	47	M	B	R	2	2	72.7
133	53	M	B	R	1	3	69.8
134	35	M	B	R	1	2	
135	65	M	B	R	1	3	61.8
136	61	M	T	R	1	0	48
137	56	M	B	R	2	3	
138	57	M	B	R	2	2	
139	62	M	B	R	2	1	
140	54	F	B	Co	2	2	63
141	55	M	B	R	1	1	
142	67	M	B	R	4	2	
143	64	M	B	R	4	3	88.4
144	59	M	B	L	2	2	29.7
145	65	M	B	R	1	2	
146	63	M	B	R	1	3	
147	83	F	B	R	2	2	
148	60	M	B	R	2	2	82.8
149	52	F	B	R	2	1	40.4
150	59	M	B	R	1	3	
151	57	M	B	R	1	3	81.1
152	56	M	B	L	1	3	76.7
153	46	F	B	R	4	2	
154	53	M	B	L	1	3	

S/N	Age	Sex	Branching	Dominance	Lesion location	Grading of coll	EF(%)
155	66	M	B	R	3	0	
156	46	M	B	R	1	2	60
157	67	M	T	R	3	2	
158	29	M	B	R	4	2	
159	42	F	T	R	1	1	
160	56	M	B	R	1	3	
161	68	M	B	R	3	0	
162	55	M	B	R	2	3	82.2
163		M	B	R	2	3	80.5
164	71	M	B	R	1	3	86.5
165	68	M	B	R	1	2	
166		F	T	R	2	2	

RESEARCH PROFILE

1. JOURNAL PUBLICATIONS

Determination of the median nerve safe-zone in the carpal tunnel using the distal forearm bony prominences
NO Ajayi, N Naidoo, L Lazarus, KS Satyapal - Folia Morphol., 73(4):409–413, 2014

Absent left main coronary artery with variation in the origin of its branches in a South African population
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
(Anat. Histol. Embryol.-Epub ahead of print- doi: 10.1111/ahe.12109*)*

The Intra-Myocardial Left Anterior Descending Artery: Incidence and Surgical Considerations in Coronary Artery Bypass Grafting
EA Vanker, **NO Ajayi**, L Lazarus, KS Satyapal- S Afr J Surg 2014;52(1):18-21

Arterial supply to the Rotator Cuff Muscles
N Naidoo, L Lazarus, BZ De Gama, **NO Ajayi** and KS Satyapal- Int. J. Morphol., 32(1):136-140, 2014

Trigeminal cave and ganglion: an anatomical review
NO Ajayi, L Lazarus, KS Satyapal- Int. J. Morphol., 31(4):1444-1448, 2013.

Anatomic parameters of the left coronary artery: An angiographic study in a South African population
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal-. Int. J. Morphol., 31(4):1393-1398, 2013

The impact of left main coronary artery anatomy on the distribution of atherosclerotic lesions in its branches.
NO Ajayi, L Lazarus**,** EA Vanker, KS Satyapal- Folia Morphol., 72(3):197-201, 2013

The Prevalence and the Clinical importance of the "Additional" Terminal Branch of the Left Coronary Artery
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal- Folia Morphol., 72(2):128–131, 2013

Multiple Variations of the Branches of the Brachial Plexus with Bilateral connections between Ulnar and Radial nerves
NO Ajayi, L Lazarus, KS Satyapal. Int. J. Morphol., 30(2):656-660, 2012

The frequency of twinning in a rural community in Western Nigeria--an update. Awojobi OA, jeje OM, Oti OO, Dania S, Dada O, Gbadamosi OA, **Ajayi NO**, Madu BE, Akanji TO, Adewumi BA. Niger Postgrad Med J. 2006 Mar;13(1): 73-4.

MANUSCRIPT IN PRESS

Arterial variations of the Subclavian-axillary arterial tree: Its association with the supply of the Rotator Cuff Muscles
N Naidoo, L Lazarus, BZ De Gama, **NO Ajayi** and KS Satyapal
(International Journal of Morphology - Manuscript number 11-14)

MANUSCRIPTS UNDER REVIEW

Preservative role of Coronary Collaterals on Left Ventricular Function: Answer to a long-standing controversy
NO Ajayi, EA Vanker, KS Satyapal
Catheterization and Cardiovascular Interventions, Manuscript # CCI-14-1621

An anatomical investigation of the carotid canal
N Naidoo, L Lazarus, NO Ajayi, KS Satyapal
Folia Morphologica, Manuscript number: #FM 38880

An anthropometric study of the tibia in the Black South Africans
N Naidoo, L Lazarus, NO Ajayi, KS Satyapal
Folia Morphologica, Manuscriot number: #FM 38938

REFEREED ABSTRACTS / SHORT PAPERS

The left coronary artery and its branches: their anatomical base for surgical intervention

NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
Proceedings of the 42nd Annual Meeting of the Surgical Research Society of Southern Africa, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, 26-27 June 2014

An anthropometric study of the tibia in a Black KwaZulu-Natal population.
L Lazarus L, N Naidoo, **NO Ajayi**, KS Satyapal
Proceedings of the 42nd Annual Conference of the Anatomical Society of Southern Africa, Stellenbosch Institute for Advanced Studies (STIAS), Stellenbosch, South Africa, 13-16 April 2014

An anatomical investigation of the carotid canal
L Lazarus L, N Naidoo, **NO Ajayi**, KS Satyapal
Proceedings of the 42nd Annual Conference of the Anatomical Society of Southern Africa, Stellenbosch Institute for Advanced Studies (STIAS), Stellenbosch, South Africa, 13-16 April 2014

An osteometric evaluation of the median nerve in the carpal tunnel and its clinical significance
Ajayi NO, N Naidoo, L Lazarus, KS Satyapal
Proceedings of the 41st Annual Conference of the Anatomical Society of Southern Africa, Department of Clinical Anatomy, University of KwaZulu-Natal, Durban, 20-24 April 2013.

Unusual variation of the brachial plexus: Bilateral ulnar and radial nerve communication
Ajayi NO, L Lazarus, KS Satyapal
Proceedings of the 41st Annual Conference of the Anatomical Society of Southern Africa, Department of Clinical Anatomy, University of KwaZulu-Natal, Durban, 20-24 April 2013.

Absent Left Main Coronary Artery: Prevalence and Clinical Relevance
Nasirudeen Ajayi, Lelika Lazarus, Ebrahim Vanker, and Kapil Satyapal
Proceedings of the 2nd International Anatomical Sciences And Cell Biology Conference, Chiang Mai, Thailand, 6-8 December 2012.

The role of left coronary artery anatomy on atherosclerotic lesion distribution in its branches
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
Proceedings of the 40th Annual Conference of the Anatomical Society of Southern Africa, University of Namibia Medical School, 14-18 April 2012

Clinically important anatomic parameters of the left coronary artery: an angiographic study
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
Proceedings of the 40th Annual Conference of the Anatomical Society of Southern Africa, University of Namibia Medical School, 14-18 April 2012

The ramus medianus artery: An entity without Identity
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
Proceedings of the 40th Annual Conference of the Anatomical Society of Southern Africa, University of Namibia Medical School, 14-18 April 2012

An evaluation of the position of the median nerve in the carpal tunnel using distal forearm bony prominences.
Ajayi NO, N Naidoo, L Lazarus, Ks Satyapal
Clinical Anatomy 26:911–917 (2013)

Composite arterio-venous grafts in coronary artery bypass surgery
Satyapal K.S. Vanker E.A., Lazarus L, **Ajayi NO**
Proceedings of the 8th Annual Conference of the Australian and New Zealand Association of Clinical Anatomists, 8-9 December 2011, Dunedin, New Zealand
Clinical Anatomy 25:530–543 (2012)

Incidence of myocardial bridges in the left anterior descending artery and relevance in coronary artery bypass graft
Satyapal KS, **Ajayi NO**, Vanker EA, Lazarus L
Proceedings of the 8th Annual Conference of the Australian and New Zealand Association of Clinical Anatomists, 8-9 December 2011, Dunedin, New Zealand
Clinical Anatomy 25:530–543 (2012)

Composite grafts in coronary artery bypass surgery: A preliminary report
Vanker EA, Lazarus L, **Ajayi NO**, Satyapal KS
Proceedings of the 39th Annual Conference of the Anatomical Society of Southern Africa, Wits Medical School, Johannesburg, 22-25 May 2011
Clinical Anatomy 24:924–935 (2011)

Myocardial bridging: Anatomical and Clinical Significance in Coronary artery bypass patients
Ajayi N.O., Vanker E.A., Lazarus L., Satyapal K.S.
Proceedings of the 39th Annual Conference of the Anatomical Society of Southern Africa, Wits Medical School, Johannesburg, 22-25 May 2011
Clinical Anatomy 24:924–935 (2011)

Ventricular Aneurysm Repair: Anatomical and Clinical Study of Non-Resection Technique
Vanker EA, **Ajayi NO**, Satyapal KS
39th Annual Conference of the Anatomical Society of Southern Africa,
Wits Medical School, Johannesburg, 22-25 May 2011

2. SCIENTIFIC CONFERENCES

PAPERS DELIVERED AT CONFERENCES

NATIONAL

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The left coronary artery and its branches: their anatomical base for surgical intervention
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
42nd Annual Meeting of the Surgical Research Society of Southern Africa,
Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, 26-27 June 2014

An osteometric evaluation of the median nerve in the carpal tunnel and its clinical significance
Ajayi NO, N Naidoo, L Lazarus, Ks Satyapal

41st Annual Conference of the Anatomical Society of Southern Africa, Department of Clinical Anatomy, University of KwaZulu-Natal, Durban, 20-24 April 2013.

Unusual variation of the brachial plexus: Bilateral ulnar and radial nerve communication
Ajayi NO, L Lazarus, KS Satyapal
41st Annual Conference of the Anatomical Society of Southern Africa, Department of Clinical Anatomy, University of KwaZulu-Natal, Durban, 20-24 April 2013.

The role of left coronary artery anatomy on atherosclerotic lesion distribution in its branches
NO Ajayi, L Lazarus, EA Vanker, KS Satyapal
40th Annual Conference of the Anatomical Society of Southern Africa,
University of Namibia Medical School, 14-18 April 2012

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39th Annual Conference of the Anatomical Society of Southern Africa,
Wits Medical School, Johannesburg, 22-25 May 2011

INTERNATIONAL

Absent Left Main Coronary Artery: Prevalence and Clinical Relevance
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