CHAPTER 3: MATERIALS AND METHODS

3.1 Study Design

A cross-sectional study

3.1.1 Study Setting

In order to get a correct representation of the South Indian population, the states of Kerala, Karnataka, Tamilnadu and Telangana were included for data collection. Hospitals were selected according to the number of cardiac patients identified by them. The collection of samples was done after procuring the sanction for the same, from the ethical committee of the pre-selected hospitals. The necessities for including more number of hospitals from each state were avoided as sufficient samples were obtained under the stipulated period from the preselected hospitals.

3.1.2 Hospitals selected as study setting

1. K. S. Hegde Medical Academy (KSHEMA), Derlakatte, Mangalore, Karnataka
2. Pariyaram Medical College (SAHAKARANA HRUDAYALAYA), Kannur, Kerala
3. Madras Medical Mission Hospital, Chennai, Tamil Nadu
4. Care hospital, Hyderabad, Telangana
Fig. 3.1 Study plan-Flow chart

**IDENTIFICATION OF HOSPITALS**

**PATIENT SELECTION**

i. Inclusion and exclusion criteria.

ii. Explanation and distribution of patient information sheet.

iii. Obtaining the informed consent, if the patient is willing to participate in the study.

**DATA COLLECTION**

i. Assessment of height and weight for BMI calculations.

ii. Obtaining QCA reports.

iii. Calculating the CAM

iv. Assessing the arteries for MB

v. Observing the coronary DP's

vi. Measuring the bridged artery at its systole, diastole and for its length.

vii. Categorizing the cases into Normal / Diseased (SVD, DVD, TVD) according to the QCA reports.

viii. To refer for the treatment suggested for diseased coronaries.

**STATISTICAL ANALYSIS AND COMPARISON**

**COMPARISON WITH THE PREVIOUS STUDIES AMONG VARIOUS RACES**

Abbreviations: QCA- Quantitative coronary angiography, BMI- Body mass index, CAM- Coronary artery measurements, MB- Myocardial bridging, DP- Dominance patterns, NCCA- Non critical coronary artery, SVD- Single vessel disease, DVD- Double vessel disease, TVD- Triple vessel disease
3.1.3 Study subjects

Patients who visited the cardiology outpatient department in the selected hospitals as a part of their routine cardiac checkups were selected as study subjects. The selection criteria were based on the patients health condition, i.e; if they undergo QCA procedure due to variation in the normal cardiac parameters. The selection criteria to be enrolled for QCA procedure were strictly subjected to the guideline protocols.

3.1.3.1 Inclusion Criteria

- All patients who had undergone QCA procedure as a part of their routine diagnosis were selected for the study purpose after obtaining the informed consent.

- The criterion was strictly subjected if the patients were of Indian origin and from the respective state. For this history of the patient origin was enquired and cross-checked with the patient details from respective files.

3.1.3.2 Exclusion Criteria

- Patients with congenital heart disease, rheumatic heart diseases, and cardiomyopathies were excluded from the study.

- Patients known to be diabetic for five or more than five years were not included in the study regardless even of having normal coronaries.

- Patients with normal looking coronary arteries after a PCI procedure and individuals with a previous history of myocardial infarction were also excluded.

3.1.4 Sample size calculation

Four thousand samples were estimated statistically for conducting the study.

a. Sample size determination

The minimum sample size required was 3,855 cases. The sample size was taken as 4,000 as the samples can be taken up to 8-10% more than that of the estimated sample
size. This also helped for an equal allotment of samples among four states. The estimated sample size was divided equally as the study was conducted in four South Indian states = 4,000/4 = 1,000 cases per state.

- Level of significance = 5%
- Effect size = 0.015
- Prevalence = 12% [54]

The sample size was estimated by consulting a statistician and with the help of the statistical software G* Power 3.0.10

**3.1.5 Sampling technique**

A technique of convenience sampling was done as all eligible cases which fulfil the inclusion criteria during the stipulated time period of the study were selected as samples. Patients were approached at the respective admission wards, for cardiac catheterization, prior to the QCA procedure.

**3.2 Methodology in detail with relevant references**

**3.2.1 Ethical considerations**

a) Ethical clearance from the Institutional Ethics Committee of Yenepoya University, as well as from the committees of the four hospitals identified for the study were obtained. The study proposal was described by a power point presentation in front of the respective committees. No major changes were amended to the initial study proposal. This was followed by the approval from the Director/ Medical Superintendent of the hospitals for the data collection (Appendix I and II).

b) Patient information sheets were provided to the patients for their better understanding about the research study. Informed written consent was obtained from the patients who were willing to participate in the study. As the study was conducted in four south Indian states, local language translated consent forms which has been translated by the language experts were provided and explained to the patient on demand (Appendix III and IV).
c) Confidentiality of the patients was maintained and they were informed that their participation and non-participation in the study would have no bearing on their treatment expenses at the hospital.

### 3.2.2 Quantitative coronary angiography (QCA) procedure principle and preparations

The principle of radiographic coronary imaging has been described below. Radiation produced by the x-ray tube gets attenuated as it passes through the human body and gets detected by the image intensifier. Iodinated contrast medium injected into the coronary arteries prior to the procedure enhances the absorption of x-rays. This produces a sharp contrast with the surrounding cardiac tissues. These x-ray shadows were converted into visible light images by an image intensifier and get displayed on fluoroscopic monitors and were stored on a digital storage system.

Digital imaging was preferred to 35-mm cine film for QCA because of its versatility with respect to image transfer, low-cost acquisition, albeit at slight lower resolution as well as easy storage and capability for image enhancement after image acquisition. Flat-panel detectors have replaced image intensifiers and have eliminated the analog-to-digital converters of the conventional image intensifiers. This advance has resulted in the reduced radiation exposure and enhanced image quality.

The major epicardial branches and their second- and third-order branches can be visualized by QCA. The network of smaller intramyocardial branches generally is not seen because of their minimal dimensions, reduced cardiac motion and also due to limited resolution of QCA systems. These fourth-order-and-beyond “resistance” vessels play a major role in the auto regulation of coronary blood flow. This may limit myocardial perfusion during stress and contribute to ischemia in patients with LV hypertrophy or systemic hypertension. Coronary perfusion of smaller branch vessels can be quantitatively assessed by use of the myocardial blush score. This has important prognostic significance in patients with ST segment elevated myocardial infarction (STEMI) and those undergoing PCI [9].
3.2.2.1 Preparation of the patient

Elective QCA was performed on eligible patients in conjunction with right-heart catheterization or contrast-enhanced left ventriculography. If any co-morbid conditions, such as congestive heart failure, diabetes mellitus or renal insufficiency were present, stable condition of the patient at the time of the procedure was ensured. A baseline electrocardiogram, electrolyte and renal function tests, complete blood cell count, coagulation panel and serum creatinine assay was ensured to be performed prior to the procedure and was reviewed before QCA [9]. QCA can be safely performed in patients on aspirin, unfractionated heparin, low molecular weight heparin, and glycoprotein IIb/IIIa inhibitors without interruption [21].

Warfarin should be discontinued 3 days before elective QCA and international normalized ratio (INR) should be 1.8 or less for femoral cases. For radial cases INR should be 2.2 or less before the procedure [21,123]. Dabigatran should be stopped 24 hours before the procedure if the glomerular filtration rate (GFR) is higher than 50 mL/min and 48 hours before the procedure, if the GFR is between 30 and 50 mL/min. Metformin should be withheld in diabetic patients before the procedure and should not be restarted after the procedure until the renal function has normalized [21].

A “time-out” check was performed at the beginning of the procedure to verify the name of the patient, the referred procedure to be performed, the signed consent, allergies, antibiotic administration, and other pertinent clinical information that can enhance patient safety [21].

3.2.2.2 Vascular Access

A variety of vascular approaches are available for QCA. They are femoral artery approach, brachial artery approach, and radial artery approach. The selection of the vascular access depends on the operator and patient preferences, anticoagulation status and the presence of peripheral vascular disease.

a. Femoral Artery Approach

The right and left femoral arteries are the most commonly used access sites for QCA. The common femoral artery passes downwards and medially first to the femoral head
then to the femoral triangle and then in the adductor canal. The femoral artery gives off three superficial and three deep branches in the femoral triangle. This can be localized by means of fluoroscopy before arterial cannulation. The anterior wall of the common femoral artery should be punctured several centimeters below the inguinal ligament but proximal to the bifurcation of the superficial femoral and profunda arterial branches.

If the puncture site is proximal to the inguinal ligament, there is an increased risk of retroperitoneal hemorrhage which is difficult to reduce with manual compression. High risk of pseudoaneurysm after the sheath removal can occur if the puncture site is at or distal to the femoral artery bifurcation. Ipsilateral cannulation of the femoral artery and femoral vein can be associated with an increased risk of arteriovenous fistula formation. Optimal femoral artery cannulation should be facilitated with vascular ultrasound guidance.

Femoral artery sheaths can be removed when the activated clotting time is less than 180 seconds. Patients should be confined to bed rest for 1 to 2 hours after the removal of a 4 French (F) (1F = 0.33-mm diameter) or 5F sheath and for 2 to 4 hours after the removal of a 6F to 8F sheath. If there is higher risk of bleeding, bed rest is advised for a day. In those cases vascular closure devices can be used [21].

b. Brachial Artery Approach

Recent studies indicate that percutaneous access to the brachial and radial arteries are most commonly used for QCA. These approaches are preferred to the femoral approach in the presence of severe peripheral vascular disease and morbid obesity. Brachial artery can easily accommodate an 8F sheath. A specific risk associated with the brachial artery approach is compromised of the blood supply to the forearm and hand in the event of a vascular complication after the procedure [124].

c. Radial Artery Approach

Radial artery access is generally preferred over the brachial artery approach. Ease of the catheter entry and removal is the benefit of the procedure. The branches of brachial artery are ulnar and radial artery. Therefore, blood supply to the hand is not hindered even if radial artery puncture is done [125,126]. An Allen test is performed
before the procedure to determine the adequacy of ulnar arterial flow, using plethysmography or by of palmar hand color assessment during manual compression of the radial artery.

Systemic anticoagulation with unfractionated heparin (up to 5000 units) or bivalirudin is used for both brachial and radial artery approaches [127]. The occurrence of radial artery spasm can be prevented by the use of hydrophilic sheath and intra-arterial administration of verapamil as well as nitroglycerin. But, rare episodes of radial artery trauma and avulsion were reported in some studies. The long-term radial artery patency rate can also be improved using a compression device which allows perfusion of the hand during hemostasis [128].

Unsuccessful transradial accesses were usually associated with several anatomic factors such as high-bifurcation radial origin, full radial loop and extreme tortuosity radial artery [129]. The radial artery approach allows improved coronary visualization, reduced bleeding complications and an immediate ambulation after QCA when compared to femoral artery approach [130]. The radial artery generally accommodates 4F to 6F catheters [9].

3.2.2.3 Catheters

Diagnostic catheters developed for QCA are generally constructed from polyethylene and polyurethane with a fine wire braid within the wall. This allows an easy advancement, better directional control (torque) and also prevents kinking. The outer diameter size of the catheters ranges from 4F to 8F. But 5F and 6F catheters are most commonly used for diagnostic QCA [9].

a. Judkins catheters

The Judkins left catheter is preshaped to allow its entry with minimal catheter manipulation into the left coronary ostium by femoral approach (Fig. 3.2). A pre-formed Judkins left catheter can also be used from the left or right brachial or radial artery. Generally, a catheter with less than 0.5 cm curvature is better suited for coronary cannulation by femoral approach. Judkins right catheter is shaped to permit entry into the RCA by minimal clockwise rotational manipulation of the catheter from any vascular approach [9].
Selection of Judkins catheter shape is based on the body habitus of the patient and the size of the aortic root. The LCA is easily engaged with the Judkins left 4F catheters through the femoral approach in most patients, whereas patients with a dilated ascending aorta may require the use of a Judkins left 5F or 6F catheter.

The best technique for the removal of a folded Judkins left catheter from the body involves withdrawing the catheter into the descending aorta and advancing a guidewire anterograde in the contralateral common iliac artery. The catheter gets straightens when both catheter and guidewire gets withdrawn together. Further, the catheter can be removed safely from the body without disruption of the arterial access site [9].

b. Amplatz Catheters

Amplatz catheters can be used for the femoral or brachial approach to QCA (Fig. 3.3). The Amplatz catheters constitute an excellent alternative in cases in which the Judkins catheter is not appropriately shaped to enter the coronary arteries. The Amplatz L-1 or L-2 catheter may be used for QCA from the right brachial or radial approach. A modified Amplatz right catheter (AR-1 or AR-2) can be used for the engagement of a horizontal or upward takeoff RCA and saphenous venous grafts (SVG’s).
Fig. 3.3 Amplatz right (R) and left (L) catheters

c. Other Catheters

Other catheters used for QCA include the internal mammary artery (IMA) left catheter with an angulated tip that allows engagement of the IMA or an upward takeoff RCA. Catheter shapes that permit engagement of SVGs include the multipurpose catheter (Fig. 3.4) and the Judkins right, modified Amplatz right, and hockey stick catheters. Specially designed catheters for engagement of the coronary arteries from the radial artery also have been developed.

Fig. 3.4 Multipurpose (MP), internal mammary (IM), and left coronary bypass (LCB) catheters
3.2.2.4 Drugs Used During QCA

a. Analgesics

Analgesics are used to achieve a state of conscious sedation, defined by a minimally depressed level of consciousness that allows the patient to respond appropriately to verbal commands and to maintain a patent airway [131,132]. Several different sedation regimens are recommended, but depending on the patient’s comorbid conditions, most operators use diazepam, 2.5 to 10 mg orally, and diphenhydramine, 25 to 50 mg orally, 1 hour before the procedure. Intravenous midazolam, 0.5 to 2 mg, and fentanyl, 25 to 50 μg, also are useful agents to provide sedation during the procedure. Patients undergoing conscious sedation should have continuous and oximetry monitoring as well as access to oxygen and suction ports and a resuscitation cart.

b. Anticoagulants

Intravenous unfractionated heparin is no longer required during routine QCA. Intravenous unfractionated heparin, 2000 to 5000 units can be given to patients at increased risk for thromboembolic complications and to those undergoing prolonged procedures (>1 to 2 minutes) using the guidewires in the central circulation. Patients undergoing brachial or radial artery catheterization also need to receive systemic anticoagulation with unfractionated heparin or bivalirudin. Frequent flushing of all diagnostic and guiding catheters with heparinized saline will prevent the formation of microthrombi within the catheter tip. A continuous flush through the arterial access sheath may also lower the occurrence of distal thrombo-embolism.

The anticoagulant effect of unfractionated heparin can be reversed with protamine, 1 mg for every 100 units of heparin. Protamine causes anaphylaxis or serious hypotensive episodes in approximately 2% of patients. This should not be administered to the patients with previous exposure to neutral protamine hagedorn (NPH) insulin, patients with a history of unstable angina or high-risk coronary anatomy and those who have undergone QCA using the brachial or radial artery.
3.2.2.5 Contrast Agents

All radiographic contrast agents contain iodine, which effectively absorbs x-rays according to the energy range of the QCA imaging system. Radiographic contrast agents currently used for QCA can cause a number of adverse hemodynamic, electrophysiologic and renal effects. The frequency of these side effects varies with different radiocontrast agents because of differences in their ionic content, osmolality and viscosity.

3.2.3 QCA procedure details

Popma et al.,(2017), have reported that QCA was initially performed even more than 30 years ago by Greg Brown and his colleagues at the University of Washington [9]. They used hand-drawn arterial contours which were corrected for pincushion distortion and reconstructed to represent a three-dimensional arterial contour. From this the reference vessel and minimal lumen diameters were measured. These initial QCA methods were time-consuming and cumbersome. Nowadays, these have been replaced with computer-assisted methods for automated arterial contour detection which has improved high speed microprocessor and enhanced storage capacity.

Visual estimations were used virtually to predict the severity of coronary stenosis in clinical practice. These “eyeball” estimates were limited by substantial observer variability and bias as well as overestimating the stenosis severity by almost 10% compared with quantitative measurements [72]. More reliable and objective “online” quantitative coronary measurements were found to have limited clinical use. Direct measurements such as fractional and coronary flow reserve measures an intermediate (40-70%) stenosis severity [133]. A number of angiographic measures have been developed to assess the early and late procedural outcome after PCI more quantitatively as well as for research protocols and registry reports.

Quantitative analysis of digital angiograms can be of two distinct processes namely, image calibration and arterial contour detection. Image calibration is accomplished using the contrast-filled diagnostic or guiding catheter as a scaling device, yielding a calibration factor in millimeters per pixel. Mapping of arterial contours begins by drawing a center line through the segment of interest. Linear density profiles are then constructed perpendicular to the center line.
A weighted average of the first and second derivative functions were used to define the catheter or arterial edges. Individual edge points were smoothed and were connected using an automated algorithm after discarding the outliers. The automated algorithm is then applied to a selected arterial segment for obtaining the absolute coronary dimensions and percent diameter stenoses were obtained. Novel quantitative algorithms have been developed recently for the measurement of smaller vessels, to assess bifurcation lesions, and to facilitate three-dimensional reconstruction [134].

Angiographic success is defined as a residual diameter stenosis less than 50% after balloon angioplasty or a diameter stenosis less than 20% after coronary stent placement. Long-term results after PCI were described using binary angiographic restenosis, which is defined as 50% or greater follow-up diameter stenosis and late lumen loss. Late lumen loss can be defined as the loss in lumen diameter during the intermediate (6- to 9-month) follow-up period. The identification of the maximal reference diameter by QCA is also useful in selecting the size of bioresorbable scaffolds for ensuring apposition to the vessel wall [135,136].

![Diagram of cranial and caudal angulated views used for QCA](image-url)

Fig. 3.5 Cranial and caudal angulated views used for QCA
3.2.3.1 QCA projections

The major coronary arteries which traverse the interventricular and atrioventricular grooves are aligned along with the long and short axes of the heart respectively. The heart is oriented obliquely in the thoracic cavity, the coronary circulation is generally visualised in the right anterior oblique (RAO) and left anterior oblique (LAO) projections (Fig 3.5). This is to furnish true anteroposterior (AP) and lateral views of the heart. But, these views are limited by vessels foreshortening of vessels and superimposition of its branches. Simultaneous rotation of the x-ray beam in the sagittal plane, namely epicranial and epicaudal projections which provide a better view of the major coronary arteries and their branches.

The relationship between the image intensifier and the patient can be explained by assuming that x-ray tube is under the patient’s table and the image intensifier is over the patient’s table. The projection is referred to as the cranial view if the image intensifier is tilted towards the head of the patient. The projection is referred to as the caudal view if the image intensifier is tilted down toward the feet of the patient. It is difficult to predict which angulated views can be the most useful for any particular patient because the “optional” angiographic projection depends largely on body habitus, variation in the coronary anatomy and location of the lesion. Coronary arteries can be visualized in both the LAO and RAO projections with both cranial and caudal angulation [9].

3.2.3.2 Selection criteria for target Vessels [137]

Standard QCA views [7,55, 138] were obtained and QCA were carried out on longest possible disease-free segments of coronary arteries which were uniformly distended and contrast-filled, free of tortuosity or kinking without overlap. The vessels were assessed in an end diastolic frame. Patients with normal coronary arteries as well as artery segments free from stenosis on angiograms were included for calibration assessment. QCA was performed for vessel diameters ranging from 0.5 mm – 7 mm.

Accesses for QCA were usually established by a percutaneous transfemoral route using the Seldinger technique. The radial artery is also an increasingly used access site. An arterial (5F/6F) sheath was inserted into the femoral artery and selective coronary catheterization were carried out with 4F/5F Judkins or Amplatz right and left
coronary catheters. All radiographic agents contain iodine; can effectively absorb x-rays in the energy range of the angiographic imaging system [9].

Selective hooking of the coronary ostium was performed and 7-8 mL nonionic contrast (Iohexol 350 mg/mL) was administrated by injection. Nitroglycerine reduces the arterial spasm by intimal smooth muscle relaxation. But, this can cause bias to the study results as it increases the diameter of the artery. No intracoronary nitroglycerine was administered prior to obtaining the images needed for the study so as to avoid the bias.

3.2.3.3 Standardized projection acquisition

Although general recommendations can be made for sequences of QCA image acquisition which are applicable in most patients, tailored views may be needed to accommodate individual variations in anatomy. As a general rule, each coronary artery should be visualized using a number of different projections that minimize vessel foreshortening and overlap. An AP view with shallow caudal angulation often is obtained first, to evaluate the possibility of LMCA disease. Other important views include the LAO cranial view to evaluate the middle and distal portions of the LAD artery. For this view, there should be sufficient leftward positioning of the image intensifier to allow separation of the LAD artery, its diagonal and septal branch. The LAO caudal view helps to evaluate the LMCA, origin of the LAD, and proximal segment of the LCx. The RAO caudal view helps to assess the LCx and its marginal branches. A shallow RAO or AP cranial view helps to evaluate the midportion and distal portion of the LAD.

RCA should be visualized in at least two views, including an LAO and RAO cranial views. LAO cranial view demonstrates the RCA, origin of the PDA and posterolateral branches. RAO view can demonstrate the mid-RCA and proximal, middle, and distal termination of the PDA. An AP cranial projection can be useful for the demonstration of the distal termination of the RCA, and a left lateral view is useful to visualize the ostium of the RCA and midportion of the RCA with separation of the RCA and its right ventricular branches.
3.2.3.4 Calibration assessments from QCA systems

Normal coronary angiograms were subsequently viewed on Volume viewer software package of GE Medical Systems USA or Siemens Artis Zeego Tech Specs systems for digital angiographic calibrations. QCA was performed using the automated coronary analysis package of the Innova 2100 IQ Cath at an AW4.4 workstation or of the SiemensQCA – Scientific coronary analysis. QCA were performed for vessel diameters ranging from 0.5 mm – 7 mm at syngo X Workplace: VB21 with acquisition at 7.5, 10, 15 and 30 f/s, acquisition for display and storage in original matrix of 12-bit (Appendix V).

Calibration assessments from QCA [27,139] systems were carried out by the same method in which the coronary catheter was employed for the QCA procedure. This incorporates the automated edge detection technique resulting in corresponding calibration factors by millimetre/pixel (mm/pixel) and the vessel contour were detected by operator independent edge detection algorithms. The dimensions of the coronary arteries were then measured using the catheter diameter (Fig. 3.6); and the absolute diameter in mm was calculated by the computerized software analysis. QCA views were selected for calibration assessment by minimising the foreshortening of the coronary segments by separating them from adjacent intervening structures.

Fig. 3.6 QCA image with an arrow pointing an intracoronary catheter by LAO caudal projections
DICOM image output on 100M bit ethernet from GE Innova 2100 IQ system with a capability of autosend and background transfer for fast transmission with minimal user interaction
All QCA images were also reviewed by two cardiologists from each centre for the definition of normal vessels and for the subsequent quantitative analysis by double blinding method. Both the observers from each centre were blinded regarding the patient identity and inter-observer variability was accounted during statistical analysis.

a. LMCA, LAD and LCx were assessed for LCA segment analysis. For LAD, ostial and proximal segment before the origin of the first septal branch ($S_1$) were measured. Measurement of the first DIAG branch was taken from a point of maximum diameter near ostium. Ostial and proximal LCx were measured around ostium and before the origin of the first OM for the proximal segment calibration assessment. The ostiums of the OM were calibrated for its measurement.

b. For RCA, the ostium and proximal segments were measured before the origin of first acute marginal (AM1) branch.

3.2.3.5 QCA reports

QCA reports were also obtained after taking the informed consents from the Interventional cardiology department cath labs of four south Indian state hospitals involved in the study for documentation. The consent forms were printed in four South Indian languages and ethical clearance from hospitals of each state, involved in the study were taken separately.

3.3 Calculation of BMI and BSA

a. BMI of a person was calculated as weight in kilograms divided by height in metres squared (kg/m$^2$).

As a measure of relative weight, BMI is easy to obtain. This is an acceptable proxy for thinness and fatness. It is directly related to health risks and death rates in many populations [140].
b. The suggested categories of BMI for Asian populations are as follows

Less than 18.5 kg/m\(^2\) - underweight

18.5–23 kg/m\(^2\) - normal / increasing but acceptable risk

23–27.5 kg/m\(^2\) - overweight / increased risk

27.5 kg/m\(^2\) or more - obesity / higher high risk [141]

c. BSA of a person was calculated from the height and the weight according to Mosteller’s formula [52].

\[
BSA = \sqrt{\frac{ht \text{ in (cm)} \times wt \text{ in (kgs)}}{3600}}
\]

d. BSA and its normal values

BSA is widely used as the biometric unit for normalizing physiologic parameters namely, cardiac output, LV mass and renal clearance. This also helps for the determination of appropriate drug dosages for chemotherapy treatments in individuals with varied body size [49,50]. The commonly accepted 50\(^{th}\) percentiles for BSA are 1.94 m\(^2\) for adult men and 1.69 m\(^2\) for adult women [51].

e. Equipments used for height and weight assessments

Weight of the patients was measured by digital weighing machine with crystal display by Health Genie digital weighing scale HD-221; silver pattern (Manufactured by Health Genie Company). Measured values were recorded as such with decimals without approximating it into highest or lowest decimal values. The height of the patient was measured by the height measuring scale with inches and centimetre calibrations by gadget Hero’s height measuring scale/tape/stature meter (200 cm /78 inch), wall mounted type (Manufactured by Gadget Hero’s company).
3.4 Data collection

Four thousand QCA reports were collected and studied for the following parameters:

i. LMCA and RCA along with its main branches were assessed for the vessel morphology at the ostium and proximal segment among normal cases by stenosis analysis programme. This programme had incorporated an automated coronary analysis package of the Innova 2100 IQ Cath at an AW4.4 workstation or of the Siemens QCA – Scientific coronary analysis. The gender wise categorisation of the data was done to denote the mean differences in the artery measurements. The SVD cases were assessed for calibrations of the non-diseased segments in the same. This helped in the regression analysis of the obtained data compared to normal (Fig. 3.7).

ii. Patient’s anthropometric measurements were done using the fore mentioned relevant equipment in the methodology. BMI and BSA were calculated. BMI was calculated by the relevant formula weight in kilograms divided by height in metres squared (kg/m\(^2\)). BSA was calculated from patient’s height and weight measurements using Mosteller’s formula. The diameters of the ten segments of coronary artery from angiogram study samples were indexed (adjusted) to BSA (mean diameter mm/m\(^2\)BSA). BMI values were correlated with indexed and non-indexed CAM of normal sample population to study the association.
ANGIOGRAM REPORTS

NORMAL

BRIDGED

DISEASED

CORONARY ARTERY DIMENSIONS WERE ASSESSED AND NOTED DOWN

CORONARY ARTERY DIMENSIONS WERE NOT ASSESSED

Fig. 3.7 Flow chart showing procedures done for data collection

Abbreviations: NCCA-Non critical coronary artery, SVD-Single vessel disease, DVD-Double vessel disease, TVD-Triple vessel disease
iii. Measurements of the diastolic and systolic phases of MB and the difference between the both were calculated to predict the relationship between increased extent of systolic compression and narrowing degree with CAD. Diameter and length of the bridging segment with the mean diameter and length of the coronary artery with bridging were measured in order to assess the percentage of bridging in the coronary artery segment.

iv. Clinical outcomes in patients with bridging by means of percentage stenosis in the coronary arteries with bridging were assessed.

v. Cardiac dominance and artery stenosis involvement as well as difference in the mean diameter of LCx and RCA among each pattern of dominance were recorded.

3.4.1 Individual segment measurement assessing patterns

a. Left Coronary Artery (LCA)

The Judkins left 4F coronary catheters are mostly used to engage the LCA. Judkins left catheter can be slightly rotated clockwise and advanced slowly to enter the left sinus of Valsalva. This permits the catheter tip to engage the ostium of the LMCA. Dilatation of the ascending aorta or unfolding of the aortic arch can result in the formation of an acute secondary angle of the Judkins left 4F coronary catheter during its advancement. The tip of the catheter should be pointed upwards, away from the left coronary ostium. Further advancement of the Judkins left catheter in this position should be avoided because it can result in the prolapse of the catheter on itself or gets folded in the ascending aortic arch.

A guidewire can be temporarily reinserted into the catheter to straighten the secondary bend. This allows the catheter advancement to the left sinus of Valsalva. A large Judkins left 5F or 6F catheters can be used if the ascending aorta is significantly dilated. The primary bend of the catheter can be reshaped by further careful advancement and by prompt withdrawal of the catheter in cases where the tip of the advancement of the catheter is beyond the ostium of the LCA without engagement. This allows the tip to “pop” into the ostium of the LCA. This method should be performed along with gentle clockwise or counter clockwise rotation which frequently permits selective engagement of the LCA. If the catheter tip is located below the
origin of the LMCA, as in the case of a smaller aortic root, a shorter Judkins left 3.5F catheters can be used to allow coaxial engagement of the LMCA.

Use of the Amplatz left catheters to cannulate the LCA requires more catheter manipulation than with the standard Judkins left catheter. In these circumstances, the broad secondary curve of the Amplatz left 1F or 2F catheter is positioned so that it rests on the right aortic cusp with its tip pointing toward the left aortic cusp. Alternating the advancement by retracting the catheter by slight clockwise rotation can allow the catheter tip to advance slowly and superiorly along the left sinus of Valsalva to enter the LMCA ostium. When the tip enters the ostium, the positions of the catheter can be stabilized usually with a slight retraction of the catheter. After the LCA ostium has been cannulated, the pressure at the tip of the catheter should be checked immediately to ensure that there is no damping or ventricularization of the pressure contour [9].

If a damped or ventricularized pressure tracing is obtained, the catheter should immediately be removed from the LCA and an attempt at repositioning should be made. If abnormal pressure recording persists, the catheter should be withdrawn from the LMCA and a non-selective injection of contrast medium into the LMCA should be performed, using the AP projection to evaluate the LMCA. If the pressure measured at the catheter tip is normal and a test injection of contrast agent suggests the absence of LMCA disease, left QCA is then performed using standard techniques. To remove the Amplatz left catheter from the LCA, the catheter should be advanced forward in the vessel to disengage its tip superiorly from the coronary ostium. Simply withdrawing the Amplatz left catheter results in deep seating of the catheter tip within the LMCA, potentially resulting in catheter-induced arterial dissection [9].

b. Left main coronary artery (LMCA)

LMCA arises from the superior portion of the left aortic sinus, just below the sinotubular ridge of the aorta. The LMCA ranges from 3 to 6 mm in diameter and may be up to 10 to 15 mm in length. The LMCA can be best visualized in the AP projection with slight (0 to 20 degrees) caudal angulation, but it was viewed in several projections with the vessel off the spine to exclude LMCA stenosis. The left anterior oblique angulation gave clear view of the ostium [9].
Diameter was taken at the midpoint between ostium and the bifurcation level into LAD and LCx by using catheter calibrations. The maximum diameter region was taken for assessment. However, in small arteries, caliber measurements were taken at or near ostium. Mean length from ostium to bifurcation point were calculated to assess whether to grade the artery as normal, short or long (Fig. 3.8). Results were tabulated according to the standard format.

c. **Left anterior descending branch of coronary artery (LAD)**

The LAD artery courses along the epicardial surface of the anterior interventricular groove toward the cardiac apex. In the RAO projection, it extends along the anterior aspect of the heart. In the LAO projections, it passes down between the right and left ventricles in the cardiac midline.

The major branches of the LAD artery are the septal and DIAG branches. The septal branches arise approximately at an angle of 90°. Branches run through the interventricular septum, in varying size, number, and distribution. The interventricular septum is the most densely vascularised area of the heart. The DIAG branches of the LAD artery pass over the anterolateral aspect of the heart and a wide variability in the number and size of DIAG branches are documented. Most patients (90%) have one to three DIAG branches. Acquired atherosclerotic occlusion of the DIAG branches can be suspected if no DIAG branches are visualised, particularly with unexplained contraction abnormalities of the anterolateral left ventricle. Visualization of the origin
of the DIAG branches often requires very steep (50 to 60°) LAO and angulated cranial (20 to 40°) skews.

In some patients, the LMCA trifurcates into the LAD and LCx arteries and the RAM [9]. When it is present, the RAM arises between the LAD and the LCx arteries. This vessel is analogous to either a DIAG branch or an OM branch, depending on its anterior or posterior course along the lateral aspect of the left ventricle. In most patients (80%), the LAD courses around the LV apex and terminates along the diaphragmatic aspect of the left ventricle. In the remaining patients, the LAD fails to reach the diaphragmatic surface, terminating instead either at or before the cardiac apex. In these circumstances, the PDA of the RCA or LCx artery is larger and longer than usual and supplies the apical portion of the ventricle.

The best angiographic projections for viewing the course of LAD were the cranial angulated LAO, AP and RAO views. LAO caudal view displayed the origin of the LAD in a horizontally oriented heart. RAO cranial view displayed the proximal, middle, distal segment of LAD and allows separation of the diagonal branches superiorly and the septal branches inferiorly. RAO caudal view helped to visualise the ostial LAD as it arises from LMCA. Visualization of the origin of the DIAG branches often required a very steep (50 to 60 degrees) LAO and angulated cranial (20 to 40°) skews.

The LAD generally has more anterior origin than the LCx in patients with separate ostia for the LAD and LCx arteries. The LAD can be engaged with the Judkins left catheter in these cases with absent LMCA cases with a paradoxical counter clockwise rotation. This rotates the secondary bend of the catheter to a posterior position in the aorta and turns the primary bend and tip of the catheter to an anterior position. The opposite maneuver is used selectively to engage the LCx selectively in the setting of separate LAD and LCx ostia. A Judkins catheter with a larger curve, such as a Judkins left 5F, selectively engages the downward coursing LCx. A catheter with a shorter curve, such as a Judkins left 3.5F, selectively engages the more anterior and superior origins of LAD [9].
The diameter calibrations of LAD were taken at the ostium and the proximal segment of LAD by using catheter calibrations. The maximum diameter region was taken for assessment. The proximal segment of LAD is the portion before the origin of the first septal branch (S). In the case of a superior origin of a DIAG, proximal segment measurements were taken between the first and second DIAG branch. Normal or diseased segments among LAD were noted down. Measurement of the first DIAG branch was taken from a point with maximum diameter near ostium (Fig. 3.9). Results were tabulated according to the standard format.

**d. Left circumflex branch of coronary artery (LCx)**

The LAO projection can give a clear view of the ostium of the LCx artery. The RAO caudal and LAO caudal projections were the best for visualization of the proximal and middle segments of the LCx and OM branches. The AP or 5 to 15° RAO caudal projections helped to visualise the origins of the OM branches [9]. More severe rightward angulation often superimposes the origins of the OM branches on the LCx. If the LCA is dominant, the optimal projection for the left PDA can be obtained in the LAO cranial view. The LCx artery also gives rise to one or two left atrial circumflex branches. These branches supply the lateral and posterior aspects of the left atrium [9].

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**Fig. 3.9 QCA images with arrows pointing LAD artery (A) and its DIAG branch (B) by RAO cranial projections**

Images procured from DICOM image output on 100M bit ethernet from GE Innova 2100 IQ system with a capability of autosend and background transfer for fast transmission with minimal user interaction
e. Right coronary artery (RCA)

RCA traverses both the atrioventricular and the interventricular grooves, multiple QCA projections are needed to visualize each segment of the RCA. The ostium is identified by the reflux of contrast material from the RCA, which also delineates the aortic root with swirling of contrast in the region of the ostium. The ostium of the RCA was evaluated in the LAO view, with or without cranial or caudal angulation. The left lateral views were also useful for visualization of the ostium of the RCA in difficult cases. The proximal RCA is generally evaluated in the LAO cranial or LAO caudal projection. But, it is markedly foreshortened in the RAO projections [9].

The RCA originates from the right anterior aortic sinus, inferior to the origin of the LCA. It passes along the right atrioventricular groove toward the crux of the heart. The first branch of the RCA is the conus artery, which arises at the RCA ostium or within the first few millimeters of the RCA in approximately 50% of patients [1]. If the ostium of the RCA is not easily located, the most common reason is that the ostium has a more superior and anterior origin than anticipated. Repeated attempts to engage the RCA should be made at a level slightly more distal to the aortic valve. Non-selective contrast agent injections in the right sinus of Valsalva may reveal the site of the origin of the RCA. Positioning of an Amplatz left catheter in the ostium of the RCA needs similar technique as Judkins right catheter. Paradoxical deep entry

Fig. 3.10 QCA images with arrows pointing LCx artery (A) and its OM branch (B) by RAO caudal projections

Images procured from DICOM image output on 100M bit ethernet of GE Innova 2100 IQ system with a capability of autosend and background transfer for fast transmission with minimal user interaction
into the RCA while attempting to withdraw the Amplatz catheter can occur in certain cases.

Removal of the catheter can be achieved by clockwise or counter clockwise rotation and by the advancement of the catheter to prolapse into the aortic sinus can be done in those cases [9]. An abnormal pressure tracing along with damping or ventricularization can be a predictor of the presence of an ostial stenosis or spasm, selective engagement of the conus branch or deep intubation of the RCA. The catheter tip should be gently rotated counter clockwise and it should be withdrawn slightly with an effort to free its tip in those cases. With persistent damping, a very small amount of contrast medium (<1 mL) can be injected carefully and the catheter immediately withdrawn in a “shoot-and-run” maneuver. This may allow for assessing the cause of damping [9].

The midportion of the RCA is best seen in the LAO cranial, RAO, and left lateral projections. The origin of the PDA and the posterolateral branches are best evaluated in the LAO cranial or AP cranial view. The midportion of the PDA can be visualised in the AP cranial or RAO projection. Cannulation of the origin of the RCA can be also performed in the LAO position. But this requires different maneuvers from those for cannulation of the LCA. Whereas, the Judkins left catheter naturally seeks the ostium of the LCA, the Judkins right or modified Amplatz catheters must be rotated to engage the RCA. This entry maneuver usually is accomplished by first passing the catheter to a point just superior to the aortic valve in the left sinus of Valsalva, with the tip of the catheter facing rightwards. The catheter is rotated clockwise and is withdrawn slightly. This forces the tip to move anteriorly from the left sinus of Valsalva to the right sinus of Valsalva below the sinotubular ridge. The entry into the RCA ostium can be easily facilitated if the catheter tip is moved suddenly to rightwards and downwards.
Diameter of RCA was taken by using catheter calibrations. The maximum diameter region was taken for assessment at ostium and the proximal segment of RCA. Proximal segment was the portion of RCA before the origin of first acute marginal (AM1) branch. Normal or diseased segment among RCA were noted down (Fig. 3.11). Results were tabulated according to the standard format.

3.4.1.2 Measuring pattern of a bridged segment

MB is usually confined to the LAD artery [54]. The bridged segment exhibits a normal caliber during diastole and precipitously constricts with each systole [55]. Right anterior RAO cranial view displays the proximal, middle, distal segment of the LAD and by allowing separation of the DIAG branches superiorly and the septal branches inferiorly. The AP view with cranial (20 to 40°) skew can give projection for the mid portion of the LAD, by separating the vessel from its DIAG and septal branches. The RAO caudal projection is also useful for visualization of the distal LAD and its apical termination [9]. The appropriate views were selected accordingly to visualise a bridged segment present in the LCxor RCA. A bridged coronary artery was documented for its location, diameter of the bridged segment in systolic and diastolic phase. This was done to assess the percentage of narrowing in the artery during systole.
The maximum diameter region was taken for assessments in case of diastolic and a minimum diameter in the case of systolic calibration. The length of a bridged segment as well as the whole length of the artery in which bridging was present was documented. The percentage of bridging in the artery was assessed using these parameters. Normal or diseased segments among bridged coronaries were noted down (Fig. 3.12, 3.13). Results were tabulated according to the standard format.
3.4.1.3 Coronary DP and assessment

The three main DP are right dominant, left-dominant and balanced or co-dominant depending on the origin of the PDA from RCA or LCx. Right dominance can be defined as the RCA crossing the posterior interventricular groove and gives rise to the PDA. The origin of the PDA and the posterolateral branches were best evaluated in the LAO cranial or AP cranial view [9].

If the LCx artery crosses the interventricular groove and gives rise to branches to the posterior right ventricular surface it was summarized as left dominance. If the LCx is dominant, the optimal projection for the left PDA was the LAO cranial. Co-dominance can be explained as branches from both the distal RCA and the distal LCx artery crosses the inferior interventricular septum. LAO cranial or AP cranial view can give an optimal projection to observe the same [9]. Normal or diseased segments among each DP were noted down. Results were tabulated according to the standard format.

3.4.1.4 Observation from the QCA data

Based on the angiogram reports, patients were categorised into normal, non-critical coronary arteries (NCCA) or with a diseased coronary arteries. If the coronary artery was totally free from stenosis, it was regarded as normal. If the percentage of stenosis was less or equal to 30-40%, those arteries were categorised as NCCA, which requires only medical treatment along with life style modifications. An artery was regarded as diseased; if the amount of stenosis was more than 50%. These arteries were again categorised into SVD, DVD or TVD based on the amount of stenosis present and the number of arteries involved. The treatments suggested by the cardiologist were noted down. This helped in regression analysis of the obtained data compared to normal. This helped to prove the rationale of the study.

3.5 Statistical analysis

- Statistical analysis of the present study was done using the SPSS software package for Windows version 22.0 (SPSS Inc., Chicago, IL). Descriptive statistics were used to present the socio-demographic data.
• Mean/median/mode with respective intervals were used to express coronary vessel dimensions and percentages. This helped for presenting categorical data.

• Appropriate parametric and/or non-parametric tests of significance for metric and categorical data were used for observing and documenting an association between independent and dependent variables.

• Coronary artery diameters were indexed (adjusted) to BSA using the formula: Mean CAM in mm / BSA m$^2$ (mean diameter mm/m$^2$ BSA).

• t-test, Pearson’s correlation, and analysis of variance (ANOVA) were used for metric data. Post-hoc tukeys test was used for multiple comparisons. Chi-square and logistic regression test were used for categorical data. A pearson coefficient ($p<0.05$) was considered as statistically significant.

• Independent variables: Gender, MB, cardiac dominance, BMI.

• Dependent variables: Coronary vessel size, CAD.

The Pearson correlation data can be interpreted as follows:

a) Based on the correlation coefficient ‘r’ value

Table 3.1 Different r values (correlation coefficient) implications

<table>
<thead>
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<th>SL.no</th>
<th>r value (correlation coefficient)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If $r \geq +0.70$</td>
<td>Very strong positive relationship (VSPR)</td>
</tr>
<tr>
<td>2</td>
<td>+0.40 to +0.69</td>
<td>Strong positive relationship (SPR)</td>
</tr>
<tr>
<td>3</td>
<td>+0.30 to +0.39</td>
<td>Moderate positive relationship (MPR)</td>
</tr>
<tr>
<td>4</td>
<td>+0.20 to +0.29</td>
<td>Weak positive relationship (WPR)</td>
</tr>
<tr>
<td>5</td>
<td>+0.01 to +0.19</td>
<td>No or negligible relationship (NR)</td>
</tr>
<tr>
<td>6</td>
<td>-0.01 to -0.19</td>
<td>No or negligible relationship (NR)</td>
</tr>
<tr>
<td>7</td>
<td>-0.20 to -0.29</td>
<td>Weak negative relationship (WNR)</td>
</tr>
<tr>
<td>8</td>
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<td>Moderate negative relationship (MNR)</td>
</tr>
<tr>
<td>9</td>
<td>-0.40 to -0.69</td>
<td>Strong negative relationship (SNR)</td>
</tr>
<tr>
<td>10</td>
<td>-0.70 or less</td>
<td>Very strong negative relationship (VSNR)</td>
</tr>
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</table>
b) Based on the strength of the correlation

**Table 3.2 Colour code interpretation**

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<th>NEGATIVE</th>
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<td>Weak negative</td>
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<tr>
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<td>Moderate negative</td>
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<td>&gt;0.7</td>
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<td>Strong negative</td>
</tr>
<tr>
<td></td>
<td>Not significant</td>
<td>Significant</td>
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