Original Article

A milestone in prediction of the coronary artery dimensions from the multiple linear regression equation

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A B S T R A C T

Bachground /aim: Coronary artery imaging is one of the most commonly used diagnostic methods. We aimed to investigate whether there is a correlation between left main coronary artery (LMCA), left anterior descending artery (LAD) and left circumflex artery (LCx) artery dimensions in normal cases and a possibility to express the coronary dimensions by multiple linear equations.
Materials and methods: Images of coronary angiograms of 925 normal cases selected from 3855 cases made up the study population (515 men and 410 women; age range, 30–75 years). The mean age of the patients was 55.50 ± 6.49 years. The mean body mass index was 24.79 ± 1.45 kg/m^2 (range, 31.30 –21.26 kg/m^2). The mean dimensions of LMCA, LAD and LCx were 4.18 ± 0.65 mm, 3.22 ± 0.63 mm and 3.07 ± 0.65 mm, respectively. Correlation between LMCA, LAD and LCx diameters was investigated. Multiple linear regression analysis was used to develop a model to elucidate the relationship between LMCA, LAD and LCx diameters.
Results: There was a strong correlation between LMCA dimensions and LAD and LCx dimensions ($r = 0.526$**, $p < 0.001$* and $r = 0.469$**, $p < 0.001$*, respectively). The positive correlation indicated that a regression analysis can be carried out by incorporating the measurements. Coronary artery dimensions were gender specific.
Conclusion: The present study explored the possibility of explaining the relationship with the LMCA and its branches by multiple linear equations, which may then be used to estimate the reference diameter of a stenosed coronary artery when the other two arteries are normal.

1. Introduction

Coronary artery disease (CAD) is the leading cause of death worldwide. Thus, coronary artery imaging is one of the most commonly used diagnostic methods. Noninvasive quantitative coronary angiography (QCA) has become an important imaging tool in the evaluation of patients with and at risk of CAD.[1,2] Invasive coronary angiography is the gold standard for establishing the presence, location and severity of CAD.[3,4] CAD is one of the most common causes of morbidity and mortality especially in the developing countries, which accounts for more than one-third of the total deaths. Coronary artery diameter is one of the most important factors that affect the procedure and outcome of percutaneous coronary angioplasty (PCI) and coronary bypass operations (CABG).[5] The lumen diameter of normal human coronary arteries and several factors affecting the lumen diameters have been studied previously in different countries on different populations.[6–9] The associated details about calibre of the coronary artery among the Indian population are limited. Similarly, confirmation of normal dimensions of the coronary artery will be troublesome if a plaque builds up as a long segment in the left anterior descending artery (LAD) or left circumflex artery (LCx) starting from the ostium. Some studies aimed to elucidate the correlation between the diameters of coronary arteries at bifurcation levels using Murray's law or Finet's formula.[10,11] In this study, we aimed to investigate whether there is a correlation between left main coronary artery (LMCA), LAD and LCx dimensions in normal cases. This

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helped us to go forward with an objective to explore the possibility of explaining the relationship with a multiple linear regression formula, which may then be used to estimate the reference diameter of a stenosed coronary artery when the other two arteries are normal.

2. Materials and methods

A cross-sectional study was conducted in four cities of South India. Hospitals were purposely selected according to the number of cardiac patients identified by them. Patients who undergo quantitative coronary angiography(QCA) procedure owing to abnormalities in the normal cardiac parameters were included after obtaining their informed consent. Quantitative coronary angiogram)images of 3855 cases who have undergone the evaluation for CAD were included by convenience sampling technique. All ethical principles for human research were followed, and ethical approval was obtained from the institutional ethics committee of the hospitals from where data were collected. A total of 2930 cases were excluded by the authors for the following reasons: presence of atheromatous changes, coronary artery luminal dilatation due to various reasons, presence of coronary artery origin abnormalities, absence of the LMCA, presence of metal artifacts such as surgical clips or pacemaker leads leading to difficulty in evaluation, and altered coronary anatomy due to operation. Thus, 925 cases made up the study population (515 men and 410 women; age range, 30–75 years). This study interpreted the data regarding coronary dimensions of patients referred by cardiologists for coronary angiograms owing to clinical symptoms along with electrocardiogram (ECG) abnormalities, a positive treadmill test or echocardiogram (ECHO) abnormalities. Hence, our population cannot be completely regarded as a true representation of the normal disease-free population of South India. However, the sample populations taken for dimension analysis were free from CAD. The age of the study subjects was given a cut-off at 75 years owing to marginal benefits marked during the follow-ups. Hence, a conservative approach is proven to be appropriate for the aforementioned age, which itself indicates a poor prognosis with an average yearly mortality rate of 33–35%.[12]

2.1. Data collection

The LMCA was best visualized in the anteroposterior projection with slight (0–20°) caudal angulation, but it was also viewed in several projections with the vessel off the spine to exclude LMCA stenosis. The left anterior oblique angulation (LAO) gave a clear view of the ostium (Fig. 1). The LAD courses along the epicardial surface of the anterior interventricular groove towards the cardiac apex. In the right anterior oblique angulation 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 (Fig. 2). The LAO projection gave a clear view of the ostium of the LCx[13] (Fig. 3).

The LMCA diameter was taken at the midpoint between the ostium and the bifurcation level into the LAD and LCx by using catheter calibrations. The maximum diameter region was taken for assessment. However, in small arteries, calibre measurements were taken at or near the ostium. The diameter calibrations of the LAD and LCx were taken at the ostium and the proximal (prox) segment of the LAD by using catheter calibrations. The maximum diameter region was taken for assessment. Normal coronary angiograms were subsequently viewed on Volume viewer software package of GE Medical Systems, USA, or on Siemens Artis Zeego Tech Specs
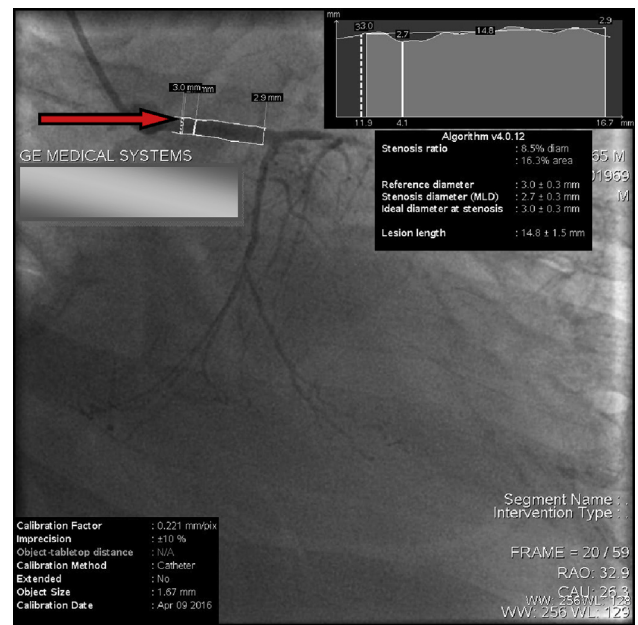

Fig. 1. QCA image with an arrow pointing the LMCA by RAO caudal projection. QCA, quantitative coronary angiography; LMCA, left main coronary artery; RAO, right anterior oblique angulation.
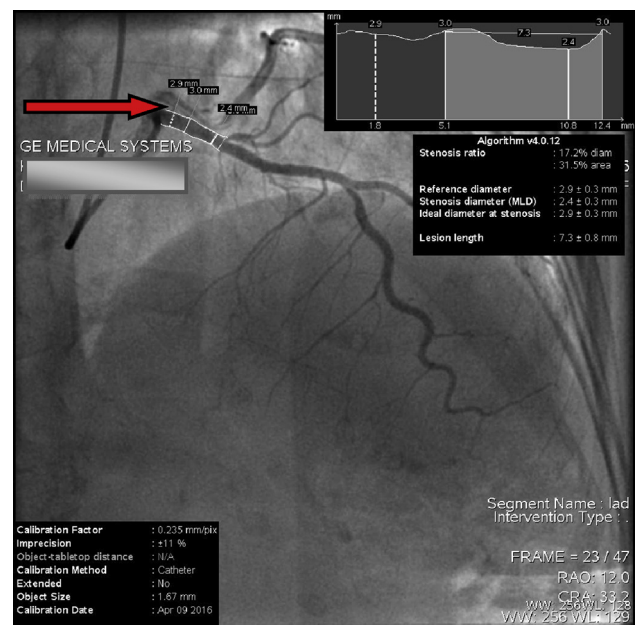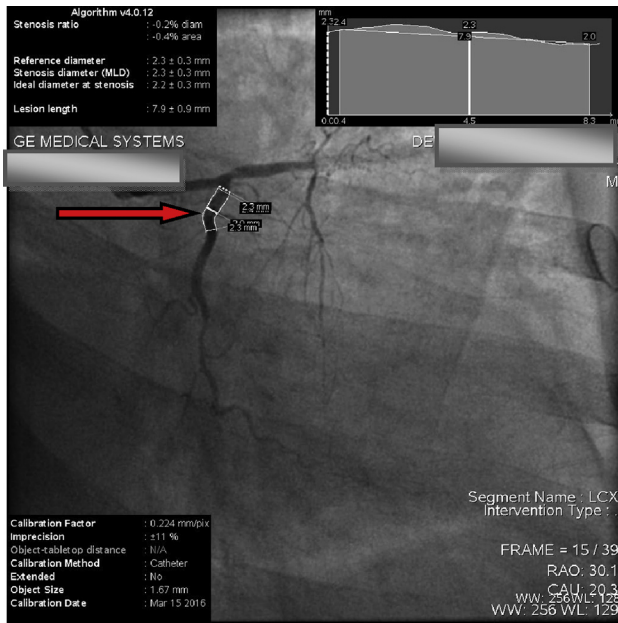

Fig. 2. QCA image with an arrow pointing the LAD by RAO cranial projections. QCA, quantitative coronary angiography; LAD, left anterior descending artery; RAO, right anterior oblique angulation.

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 Siemens QCA – Scientific coronary analysis. QCA was performed for vessel diameters ranging from 0.5 mm–7 mm using the *syngo* X Workplace: VB21 with acquisition at 7.5, 10, 15 and 30 f/s, acquisition for display and storage in the original matrix of 12-bit. Calibration assessments from QCA[14,15] systems were carried out by the same method in which the coronary catheter was used for the QCA procedure. This incorporates the automated edge detection technique, resulting in

Fig. 3. QCA image with an arrow pointing the LCx by RAO caudal projections. QCA, quantitative coronary angiography; LCx, left circumflex artery; RAO, right anterior oblique angulation.

the corresponding calibration factors by millimetres/pixels, and the vessel contour was detected using the operator-independent edge detection algorithms. The dimensions of the coronary arteries were then measured using the catheter diameter, and the absolute diameter in millimetres was calculated by computerized software analysis. 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 the double blinding method. Both the observers from each centre were blinded regarding the patient identity, and interobserver variability was accounted during statistical analysis.

2.2. Statistical analysis

Statistical analyses were conducted using SPSS software version 22.0. Normal distribution of the variables was ensured using visual (histograms and probability plots) and analytical methods. Normally distributed variables were presented using means and standard deviations. Correlation between LMCA, LAD and LCx diameters was investigated using the Pearson correlation coefficient. Student's t-test was used to compare LMCA, LAD and LCx diameters between males and females. Multiple linear regression analysis was used to develop a model to elucidate the relationship between LMCA, LAD and LCx diameters. The model fit was assessed using appropriate residual and goodness-of-fit statistics. A series of regression analyses were run to compare the fitness of the model between genders; Fisher's Z test was performed, and R^2 values were compared.

3. Results

The mean age of the patients was 55.50 ± 6.49 years. Physical and demographic parameters were assessed. The average weight was 65.20 ± 3.09 kg (range, 90.00–37.00 kg) and height was 171.15 ± 5.20 cm (range, 190.00–135.00 cm). The body mass index (BMI) and body surface area (BSA) of the normal samples were calculated. The mean BMI was 24.79 ± 1.45 kg/m^2 (range, 31.30–21.26 kg/m^2). The mean dimensions of the LMCA, LAD and

LCx were 4.18 ± 0.65 mm, 3.22 ± 0.63 mm and 3.07 ± 0.65 mm, respectively. In subgroup analysis of genders, LMCA, LAD and LCx diameters were calculated as 4.11 ± 0.62 mm, 3.14 ± 0.59 mm and 2.99 ± 0.68 mm in women and 4.25 ± 0.67 mm, 3.29 ± 0.67 mm and 3.15 ± 0.61 mm in men, respectively. We compared coronary artery dimensions among both genders and found a statistical difference for all segments taken for the assessments ($p < 0.001^*$) as well as between the models.

No correlation was found between coronary artery dimensions and patients' age. Similarly, there was a negative correlation between coronary dimensions and BMI (LMCA$\underline{r} = -0.150^{**}$, $p = <0.001^*$; LAD$\underline{r} = -0.135^{**}$, $p = <0.001^*$ and LCx$\underline{r} = -0.191^{**}$, $p = <0.001^*$). There was a strong correlation between LMCA dimensions and LAD and LCx dimensions ($\underline{r} = 0.526^{**}$, $p < 0.001^*$ and $\underline{r} = 0.469^{**}$, $p < 0.001^*$, respectively).

Regression analysis revealed the following formula. There was a gender-specific difference between the predicted equations.

A multiple linear regression was calculated to predict LAD-o (ostium) based on the LMCA and LCx-o for females.

The participant-predicted equation for females is as follows *LAD-o*=0.953 + 0.349*LMCA+0.244*LCX-o.
- For every unit increase in the LMCA, we expect a 0.349-mm increase in LAD-o, holding all other variables constant, and for every unit increase in LAD-o, we expect a 0.244-mm increase in LCx-o, holding all other variables constant ($p < 0.001$; with an R^2 of 0.706) (Graph 1).

A multiple linear regression was calculated to predict LAD-o (ostium) based on the LMCA and LCx-o for males.

The participant-predicted equationfor males is as follows: *LAD-o*=0.971 + 0.393*LMCA+0.196*LCX-o.
- For every unit increase in the LMCA, we expect a 0.393-mm increase in LAD-o, holding all other variables constant, and for every unit increase in LAD-o; we expect a 0.196-mm increase in LCx-o, holding all other variables constant ($p < 0.001$; with an R^2 of 0.637) (Graph 2).
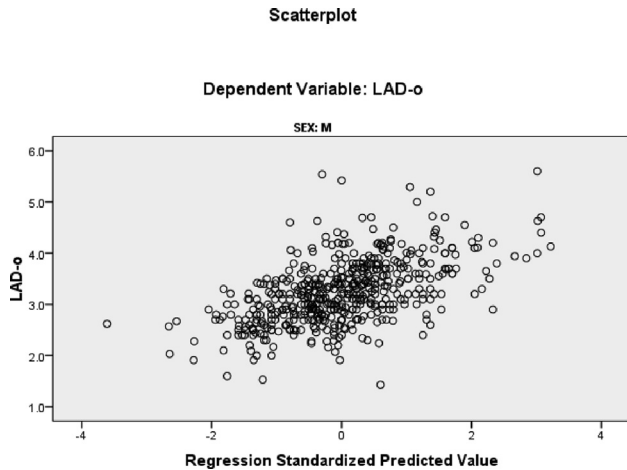
A multiple linear regression was calculated to predict LCx-o (ostium) based on the LMCA and LAD-o for females.

The participant-predicted equation for females is as follows: *LCx-o*= 0.796 + 0.326*LMCA+0.271*LAD-o.
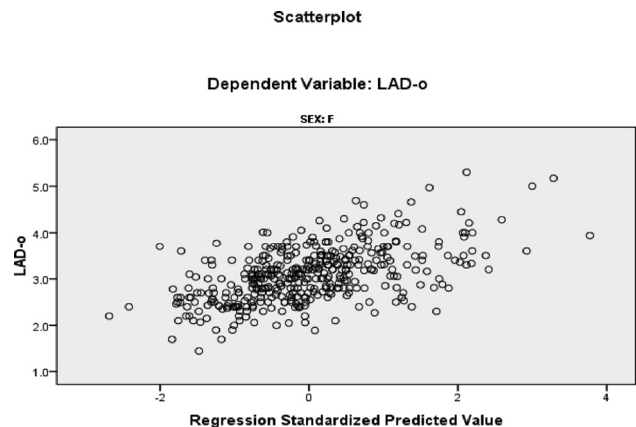
Graph 1. Participant-predicted equation for females: *LAD-o*=0.953 + 0.349*LMCA+0.244*LCx-o. LAD-o, left anterior descending artery ostium; LAD, left anterior descending artery; LMCA, left main coronary artery; LCx-o, left circumflex artery ostium.

Graph 2. Participant-predicted equation for males: *LAD-o*=0.971 + 0.393*LMCA+0.196*LCx-o. LAD-o, left anterior descending artery ostium; LAD, left anterior descending artery; LMCA, left main coronary artery; LCx-o, left circumflex artery ostium.

Graph 4. Participant-predicted equation for males: *LCx-o*= 1.206 + 0.290*LMCA+0.208*LAD-o. LCx, left circumflex artery; LMCA, left main coronary artery; LAD-o, left anterior descending artery ostium; LCx-o, left circumflex artery ostium.
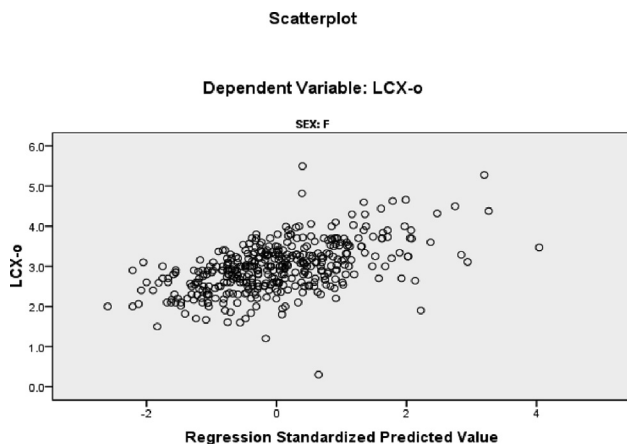
- For every unit increase in the LMCA, we expect a 0.326-mm increase in LCx-o, holding all other variables constant, and for every unit increase in LCx-o, we expect a 0.271-mm increase in LAD-o, holding all other variables constant ($p < 0.001$; with an R^2 of 0.683) (Graph 3).

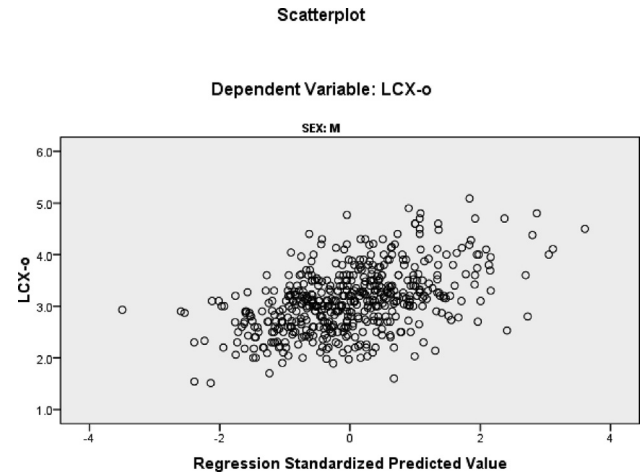**A multiple linear regression was calculated to predict LCx-o (ostium) based on the LMCA and LAD-o for males.**

The participant-predicted equation for males is as follows: *LCx-o*= 1.206 + 0.290*LMCA+0.208*LAD-o.
- For every unit increase in the LMCA, we expect a 0.290-mm increase in LCx-o, holding all other variables constant, and for every unit increase in LCx-o, we expect a 0.208-mm increase in LAD-o, holding all other variables constant ($p < 0.001$; with an R^2 of 0.729) (Graph 4).

Among all predictions, both of the predictor variables are significant with $p < 0.05$, which indicates both the variables are significantly contributing to the dependant variable.

Graph 3. Participant-predicted equation for females: *LCx-o*= 0.796 + 0.326*LMCA+0.271*LAD-o. LCx, left circumflex artery; LMCA, left main coronary artery; LAD-o, left anterior descending artery ostium; LCx-o, left circumflex artery ostium.

4. Discussion

In this study, we measured LMCA, LAD and LCx dimensions, and the intercorrelation between them was investigated. The study revealed a correlation that can be formulated between the diameters of these three arteries. The positive correlation indicated that a regression analysis can be carried out by incorporating the measurements. Knowing the dimensions of a coronary artery is crucial for appropriate stent sizing. Inappropriate measurements can predispose the patients to a higher rate of post-PCI complications such as in-stent restenosis within 6 months of the procedure. Increased mortality in women after revascularization has been attributed to gender-related differences in the coronary size,[5,16] and the artery size can be related to the outcomes after PCI.[17,18] van der Waal et al[10] and Zhou et al[19] reported geometry of the ideal bifurcation is described by Murray's law, which states that the cube of the radius of a parent vessel equals the sum of the cubes of the radii of the daughters. Both studies using this law at the LMCA branching level reported that it was successful in defining coronary artery diameters.[10,19]

Saikrishna et al[6] mentioned a positive correlation between the size of the LMCA and the prox LCx and distal LCx, the prox, mid and distal LAD and the left posterior descending artery (PD) in left-dominant circulation. In right-dominant circulation, there was a linear correlation between the diameter of the prox right coronary artery (RCA) and the mid, distal RCA and its right posterior descending (PD) and posterior left ventricular (PLV) branches. Shukri et al[20] revealed a strong positive correlation between the diameter of the LMCA and the diameters of both the prox LAD and LCx using Pearson's correlation coefficient of LAD 0.623**(mm) and LCx 0.428**(mm). Verim et al[21], reported a strong correlation between the LMCA cross-sectional area and LAD and LCx cross-sectional areas (r = 0.779, $p < 0.001$ and r = 0.678, P < 0.001, respectively) at the bifurcation level, and a regression equation was formulated to predict LMCA dimensions (LMCA = 3.870 + 0.718 × LAD + 0.434 × LCx). But the present study reveals that the equation cannot be unique for the LMCA as the cases for left main with single stents are limited. The LMCA and its branches need to be assessed throughly and the equation is gender specific.

Leung et al[9] found that determinants of coronary vessel dimensions are total or regional left ventricular mass, age and body

surface area by multivariate regression analysis. Total left ventricular mass was used for total coronary cross-sectional area (TCSA) because the percent territory score corresponding to TCSA was 100%. Multiple regression equations were formulated with mean diameters of LMCA, prox LAD and prox LCx. A territory fraction was added for age of the patient. Age factor was not added as a territory fraction in the present study because there was no correlation found between coronary artery measurements and the patient's age. Similar findings were reported in studies by Hutchins et al[22] and Zeina et al.[23] Some other studies found a slight increase in coronary arteries with age,[24,25] and a study reported age-related decrease in vasodilatation of the arteries.[9] However, the sample sizes were small in these studies to draw appropriate conclusions; the present study had a larger sample size among a wider cross section of people.

Rodriguez and Robbins[26] measured the volume of barium sulphate-gelatin injected into postmortem coronary arteries and found that there was a significant linear relationship between the sums of the cross-sectional areas of the major coronary arteries (prox LAD and prox LCx) and the capacities of the coronary arterial tree. Studies investigating cross-sectional areas of coronary arteries were mainly carried out with the purpose of investigating the LMCA. In our study, we found the dimensions of the LMCA, LAD and LCx, which can have a wide clinical perspective. Zeina et al[23] reported the distal LMCA sectional area to be 14 ± 5 mm^2 in an multiple-detector computed tomography (MDCT) study. However, Christensen et al[27] found the LMCA cross-sectional area to be 12.4 ± 4.4 mm^2, which is smaller than that reported in the study by Zeina et al.[23] The present study suggests it is better to take coronary artery measurements in diameter calibrations than the cross-sectional area as the former can help to calculate the dimensions of the coronaries during the PCI procedures more easily and to compare them with normal dimensions. This in turn can help to assign the stent size in a diseased artery according to the grade of stenosis.

Gender-wise analysis of coronary artery dimensions in the present study showed a significant difference between the coronary artery measurements among males and females. In addition, multivariable regression modelling revealed that both height and sex were strong independent predictors of the coronary vessel size.[7] However, this finding has not been consistent, and some studies have found no significant difference in normal coronary artery cross-sectional areas between genders.[14,23,28]

There was a negative correlation between coronary dimensions and the BMI in the present study. Yasmin et al has also reported a gender-specific and age-dependant significant correlation among male samples between the RCA diameter and BMI.[29] This is plausible because higher the BMI, more the fat deposit and smaller the coronary dimensions. Smaller coronaries would theoretically require a lower atheroma burden to develop stenosis, thereby leading to premature CAD. The risk of cardiometabolic multimorbidity increases as the BMI increases. Risk severity was observed more in obese and moderately to severely overweight people compared with individuals with a healthy BMI.[30]

In conclusion, the present study explored the possibility of explaining the relationship with the LMCA and its branches by a formula, which may then be used to estimate the reference diameter of a stenosed coronary artery when the other two arteries are normal.

4.1. Limitations of the study

Larger ostial diameters for the LMCA, LAD and RCA can be expected in the presence of progressive hypertension as these segments are more directly affected by the pressure rise in the aorta. It would be better if the coronary artery measurements (CAM) of the present study could have been corrected for the presence of left ventricular (LV) hypertrophy.

Conflict of interest

All authors have none to declare.

Author contributions

All authors hereby declare that their contribution was equal towards the formation of the manuscript.

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