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Original Article

Coronary artery size in North Indian population – Intravascular ultrasound-based study

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A B S T R A C T

Objective: The coronary artery dimensions have important diagnostic and therapeutic implications in management of coronary artery disease (CAD). There is paucity of data on the coronary artery size in the Indian population as measured by intravascular ultrasound (IVUS).
Methods: A total of 303 patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) with intravascular ultrasound underwent analysis along with quantitative coronary angiography (QCA). Of the 492 proximal coronary segments; 221 relating to left main (LM), 164 to left anterior descending artery (LAD), 45 to left circumflex artery (LCX), and 62 to right coronary artery (RCA) were considered.
Results: Patient's mean age was 53.37 ± 3.5 years; men 80%; hypertension 35% and diabetes 24.8%. On IVUS, mean minimal lumen diameter as compared to QCA in LM (4.60 mm versus 4.50 mm, $p < 0.001$), LAD (3.71 mm versus 3.45 mm, $p < 0.001$), LCX (3.55 mm versus 3.16 mm, $p < 0.001$) and RCA (3.85 mm versus 3.27 mm, $p < 0.001$) were significantly larger. Lumen and external elastic membrane (EEM) cross-sectional area (CSA) were larger in males as compared to females with statistical significance for lumen CSA in LM ($p = 0.04$); RCA ($p = 0.02$) and EEM CSA in LM ($p = 0.03$); RCA ($p = 0.006$) but no significance for adjusted body surface area (BSA). In multivariate models, BSA and age were independent predictors of LM and LAD diameters and areas, but age was an independent predictor indexed to BSA.
Conclusion: The coronary artery dimensions by IVUS are significantly larger than QCA. No gender difference in coronary artery size. Age was an independent predictor of coronary artery size in left main and LAD. The coronary artery size may not be a risk factor for acute coronary syndrome.

1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality in India. A quarter of all mortality is attributable to CVD, with ischemic heart disease being the predominant cause.[1] The coronary artery size in the general population is variable with multiple factors playing a crucial role such as age, gender, body habitus, genetic, environmental and life style. The outcomes after percutaneous coronary interventions (PCIs) and coronary artery bypass graft surgery (CABG) are mainly determined by the coronary artery size. Intravascular ultrasound (IVUS) is the most widely used intracoronary imaging tool for the quantitative assessment of coronary artery disease, which yields more accurate measurements of vessel geometry and lesion severity than conventional quantitative coronary angiography (QCA).[2] There are no data on the size of normal coronary arteries in the Indian population as measured using IVUS. The primary aim of this study was to determine the coronary artery dimensions by intravascular ultrasound and influence of age, gender, body surface area, diabetes, and hypertension on coronary artery size.

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2. Methods

This is a single-center observational study.

2.1. Objectives

1. To determine the normal dimensions of disease-free coronary artery segments by using intravascular ultrasound.
2. To assess the effect of age, gender, body surface area, diabetes, and hypertension on coronary artery size.

2.2. Study population

This was a single-center observational study carried out in the Department of Cardiology of a tertiary care hospital in North India. From June 2016 to Feb 2019, a total of 303 patients with acute coronary syndrome, who underwent coronary angiography followed by percutaneous coronary intervention with intravascular ultrasound guidance and had proximal disease-free coronary artery segments or minimal atheroma (<20% cross-sectional narrowing to nullify the remodeling effect) were included. Patients with deranged renal function, tortuous coronary vessels precluding IVUS examination, past history of PCI or CABG, and refusal of consent were excluded. All participants provided a written informed consent and study approved by the institutional ethics committee. All procedures were conducted in accordance with principles outlined in the Declaration of Helsinki.

2.3. PCI procedure

All patients were given 325 mg aspirin, clopidogrel 300 mg or prasugrel 60 mg along with intravenous doses of unfractionated heparin titrated to achieve therapeutic range activated clotting time prior to percutaneous coronary intervention procedure. IVUS pull back was taken using a 20-MHz, 2.9 French, Eagle Eye® Platinum RX digital IVUS catheter (Eagle Eye, Philips Volcano, San Diego, CA, USA). All patients were administered 200 mcg of intracoronary nitroglycerine, and IVUS pull back was taken starting 15 mm distal to the lesion till the aorto-ostial junction using an automatic pull back at a speed of 0.5 mm/s before any balloon dilatation. PCI was performed as per standard procedure.

2.4. Angiographic analysis

Coronary angiography was performed in all patients at a frame rate of 15/sec. Standard angiographic views were obtained and all captured angiographic images were analyzed offline. The arteries measured were the proximal left main (LM), left anterior descending (LAD), and left circumflex (LCX) in the right anterior oblique (RAO) 30° projection, and for the right coronary artery (RCA) left anterior oblique (LAO) 60° projection. The proximal coronary artery segments were considered: (1) proximal LAD segment before the first septal, (2) the proximal LCX segment before the obtuse marginal (OM), (3) the proximal RCA segment before the first right ventricular branch. A computer-assisted, automatic contour detection using software Medis Q Angio® XA 7.3 (Medis medical imaging systems, Leiden, the Netherlands), was performed. The outer diameter of the contrast filled catheter served as the calibration standard. Quantitative coronary angiography was carried out in end-diastole when coronary artery segment was contrast filled, uniformly distended and free of tortuosity or overlap.

2.5. Gray-scale IVUS analysis

The IVUS images of all the patients were recorded and stored on a DVD-ROM for offline analysis, which was performed by two independent observers (SK and RK) who were unaware of the patient details or coronary angiograms. A consensus was obtained if there was discordance in the analyses by repeated off line readings. Quantitative and qualitative IVUS analyses were performed in accordance with the American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies.[3] All the IVUS analysis was done using a validated and computerized INDEC's Echo plaque 4.3.12J software (INDEC Medical systems, Inc., Santa Clara, CA, USA). After automatic border detection for the lumen and media-adventitia interface by the software, manually correction and confirmation done, to obtain the results calculated and displayed automatically. Lumen cross sections were measured in the disease-free or minimal atheroma segments within 10–15 mm from the ostium before any side branch. After measuring the external elastic membrane (EEM) and lumen cross-sectional areas (CSAs), plaque and media (P&M) CSA was calculated as EEM minus lumen CSA. Plaque burden was estimated as plaque and media CSA divided by EEM CSA multiplied by 100.

2.6. Statistical analysis

All the statistical analysis was done using SPSS version 22.0 (SPSS, Inc., Chicago, Illinois). Categorical data were presented as percentages (%) and frequencies, and Chi-squared test or Fisher's Exact test was used as appropriate. Distribution of the continuous variables was analyzed by Kolmogrov–Smirnov test and presented as mean with standard deviation if normally distributed and median with 25th and 75th percentiles when skewed distribution. Correlations were estimated by Pearson correlation coefficient. Univariate analysis was performed to find association of categorical variables between the two study groups using either Chi-squared test or Fisher's Exact test as appropriate. Continuous variables were compared in the groups by independent t test when normally distributed and Mann Whitney U test with skewed distribution. A stepwise multiple linear regression analysis was done to determine whether age, body surface area, gender, diabetes, or hypertension was independently associated with coronary size. As body size is a confounding variable for coronary size, multiple regression analysis was again performed with the dependent variables in each model, corrected for BSA. A p value < 0.05 was considered statistically significant.

3. Results

A total of 303 patients were examined, out of which 244 were males and 59 were females. Of the 492 proximal coronary segments analyzed include, LMCA (221 sites), proximal LAD (164 sites), proximal LCX (45 sites), and proximal RCA segments (62 sites). The mean age of the patients was 53.37 ± 3.5 years (range 22–90 years). The baseline clinical characteristics of the patients are outlined in Table 1.

The mean diameter of vessels as assessed by IVUS was largest in left main, followed by proximal RCA, proximal LAD, and proximal LCX. There was a strong concordance between IVUS versus quantitative coronary angiography minimal lumen diameter (QCA MLD) in the LM, LAD, LCX, and RCA, separately (Table 2). The IVUS determined coronary artery diameter when indexed to body surface area of left main, proximal LAD, proximal LCX and proximal RCA were 2.64 ± 0.40 mm/m^2, 2.15 ± 0.35 mm/m^2, 2.05 ± 0.30 mm/m^2 and 2.20 ± 0.36 mm/m^2 respectively (Table 2).

Table 1
Baseline characteristics of the patients.

Parameter	Total (n = 303)	Males (n = 244)	Females (n = 59)
Age (years)	53.4 ± 3.5	52.6 ± 11.5	56.36 ± 12.1
Height (cm)	163.5 ± 8.38	165.7 ± 7.2	154.5 ± 6.7
Weight (kg)	68.26 ± 11.60	69.2 ± 11.3	64.3 ± 12.1
BMI (kg/m^2)	25.56 ± 4.15	25.23 ± 4.02	26.9 ± 4.5
BSA (m^2)	1.76 ± 0.17	1.78 ± 0.16	1.66 ± 0.17
Diabetes, n (%)	75 (24.8%)	51 (20.9%)	24 (40.7%)
Hypertension, n (%)	106 (35%)	71 (29%)	35 (59%)
Current Smokers, n (%)	104 (34.3%)	102 (41.8%)	2 (3.4%)
Current Alcoholics, n (%)	83 (27.4%)	83 (34%)	0
Hemoglobin (mg/dL)	13.04 ± 2.07	13.43 ± 1.99	11.34 ± 1.45
Creatinine (mg/dL)	1.05 ± 0.26	1.05 ± 0.24	1.07 ± 0.33
TC (mg/dL)	154.95 ± 51.95	154.47 ± 48.34	157.33 ± 63.84
TG (mg/dL)	137.6 ± 61.05	134.86 ± 59.83	151.02 ± 65.79
LDL (mg/dL)	95.19 ± 48.50	95.30 ± 44.63	94.68 ± 63.68
HDL (mg/dL)	40.17 ± 14.49	39.49 ± 13.34	43.26 ± 18.74

All values are presented as Mean ± SD or number (%).
BMI=Body mass index, BSA=Body surface area, TC = Total cholesterol, TG = Triglycerides, HDL=High density lipoprotein, LDL = Low density lipoprotein.

Table 2
Comparison of MLD by IVUS and QCA.

Dimension	MLD by IVUS	MLD by QCA	R-value	*p*-value
Unadjusted MLD (mm)				
Left Main	4.60 ± 0.69	4.50 ± 0.79	0.332	<0.001
pLAD	3.71 ± 0.60	3.45 ± 0.63	0.479	<0.001
pLCX	3.55 ± 0.56	3.16 ± 0.47	0.302	<0.001
pRCA	3.85 ± 0.62	3.27 ± 0.56	0.649	<0.001
Adjusted to BSA, MLD (mm/m^2)				
Left Main	2.64 ± 0.40	2.53 ± 0.57	0.376	<0.001
pLAD	2.15 ± 0.35	1.94 ± 0.48	0.253	0.016
pLCX	2.05 ± 0.30	1.72 ± 0.22	0.278	0.17
pRCA	2.20 ± 0.36	1.86 ± 0.32	0.749	<0.001

All values are presented as Mean ± SD.
MLD = Minimal lumen diameter, IVUS = intravascular ultrasound, QCA = quantitative coronary angiography, BSA = body surface area.

On IVUS, males had larger coronary artery diameter as compared to females (Fig A1). In females, the diameters were smaller than males in LM by 0.18 mm, in LAD by 0.08 mm, in LCX by 0.27 mm, and in RCA by 0.40 mm. However, it was statistically significant only in RCA. When the coronary artery size was indexed to the BSA, there was no statistically significant difference except in LCX (Fig A2).

Lumen and EEM cross-sectional areas were larger in males in comparison to females and achieved statistically significance in both left main and RCA. However, there was no statistical significance for adjusted BSA (Table 3).

On multiple linear regression analyses, the body surface area was an independent predictor of MLD in all vessels except RCA, and age was significant in both LM and LAD. However, analyses were performed for indexed MLD, as body size was a potential confounding variable, age was an independent predictor for LM ($\beta = 0.269$, 95% confidence interval [CI] 0.004–0.015 and $p < 0.001$), and LAD ($\beta = 0.234$, 95% CI 0.001–0.012 and $p = 0.01$). Similar to findings with diameters, body surface area was also an independent predictor for external elastic membrane cross-sectional area (EEM CSA), except in RCA and age, was statistically significant in both LM and LAD. When analysis performed for indexed EEM CSA, age was an independent predictor for LM ($\beta = 0.255$, 95% CI0.03–0.12 and $p = 0.001$) and LAD ($\beta = 0.30$, 95% CI 0.03–0.10 and $p = 0.001$), and hypertension was an independent predictor in LAD ($\beta = 0.208$, 95% CI 0.13–2.1 and $p = 0.027$) (Table 4). In case of LCX and RCA, no independent predictors were found for luminal

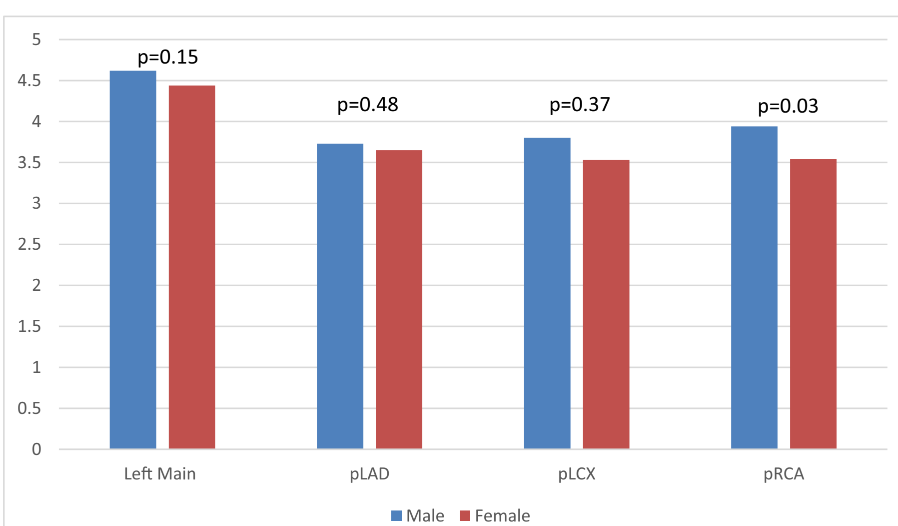

Fig A1. Coronary artery diameter by IVUS (mm), without reference to body surface area.

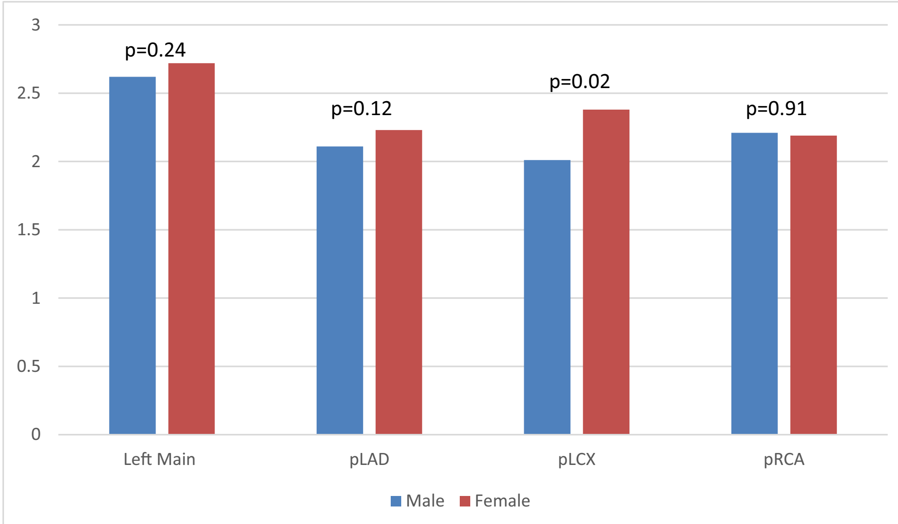

Fig A2. Coronary artery diameter by IVUS (mm) indexed to body surface area.

diameters and EEM CSA. Neither gender nor diabetes independently correlated with any of the measured arterial areas (Table S1-S3, Supplementary data).

4. Discussion

The key findings of this study are as follows: (1) intravascular ultrasound (IVUS)-measured coronary artery dimensions are significantly larger than those measured by quantitative coronary angiography (QCA); (2) minimal luminal diameters and EEM cross sectional areas are larger in males; (3) no gender difference in lumen and EEM cross sectional areas when adjusted to BSA; and (4) age was an independent predictor of coronary artery size and area in LM and LAD.

The absolute size of coronary artery segments does matter during interventional or surgical procedures. Majority of the lesions in acute coronary syndromes involve the proximal segments of the coronary arteries and jeopardize significant amount of myocardium.[4–6] The knowledge of the dimensions helps in choice of devices and stents during the coronary interventions. Smaller arteries tend to decrease the atheroma burden required to develop significant obstructive coronary lesions and further potentiates technical challenges during surgical or interventional procedures.[7]

Coronary angiogram is an established method for assessing the extent and severity of disease but has several limitations.[8] Multiple studies have shown a considerable variability in the visual interpretation of cine-angiograms.[9–11] QCA involves computerized analysis of digital images and automatic edge detection algorithms, but the validity of this angiographic quantification is also questionable.[10–12] Various discrepancies have been observed between coronary angiograms and findings on postmortem examinations.[13] One of the main advantages of IVUS imaging is its ability to precisely define the vessel dimensions and areas.

The coronary artery size is highly variable in the normal population.[14,15] Genetic factors, age, gender, body weight, body surface

Table 3
Comparison of Lumen and EEM Cross sectional area by IVUS.

Dimension	Males (n = 244)	Females (n = 59)	*p*-value
Unadjusted Lumen CSA (mm^2)			
Left Main	20.03 ± 5.93	18.41 ± 3.83	0.04
pLAD	12.79 ± 4.08	12.15 ± 3.84	0.39
pLCX	11.68 ± 3.78	12.74 ± 1.33	0.59
pRCA	13.96 ± 4.29	11.19 ± 3.07	0.02
Adjusted to BSA, Lumen CSA (mm^2/m^2)			
Left Main	11.37 ± 3.14	11.55 ± 2.61	0.80
pLAD	7.36 ± 2.15	7.69 ± 2.32	0.50
pLCX	6.69 ± 2.06	7.97 ± 0.81	0.23
pRCA	7.82 ± 2.60	6.95 ± 1.89	0.27
Unadjusted EEM CSA (mm^2)			
Left Main	25.11 ± 6.43	23.16 ± 4.42	0.03
pLAD	16.98 ± 4.87	15.94 ± 4.76	0.25
pLCX	15.56 ± 5.07	17.01 ± 2.89	0.58
pRCA	18.44 ± 4.79	14.66 ± 3.29	0.006
Adjusted to BSA, EEM CSA (mm^2/m^2)			
Left Main	14.22 ± 3.47	14.26 ± 2.93	0.95
pLAD	9.77 ± 2.55	10.13 ± 2.67	0.53
pLCX	8.91 ± 2.85	10.60 ± 1.29	0.26
pRCA	10.18 ± 2.92	9.14 ± 2.03	0.24

All Values are presented as Mean ± SD.
EEM-external elastic membrane, IVUS = intravascular ultrasound, CSA = cross sectional area, BSA = body surface area.

Table 4
Multiple linear regression models predicting EEM CSA, indexed for BSA.

Characteristic	β	*p*-value
LM model		
Age	0.255	0.001
Gender	−0.047	0.54
Diabetes	−0.029	0.70
Hypertension	0.096	0.21
LAD model		
Age	0.300	0.001
Gender	−0.093	0.33
Diabetes	−0.018	0.84
Hypertension	0.208	0.03
LCX model		
Age	0.136	0.47
Gender	0.122	0.56
Diabetes	0.107	0.60
Hypertension	−0.019	0.92
RCA model		
Age	0.204	0.19
Gender	−0.140	0.38
Diabetes	−0.116	0.45
Hypertension	−0.112	0.48

BSA=Body surface area, LM = Left main coronary artery, LAD = Left anterior descending artery, LCX = Left circumflex artery, RCA = Right coronary artery.

area, weight of the heart, ethnicity, race and environmental factors, have all been correlated with the coronary artery size.[15–21] Smaller coronary artery size has been reported in Indians as compared to the western counterparts.[21,22] This has been attributed to the body habitus and relatively smaller body surface area.[22] Raut et al., observed similar findings, where in coronary artery diameters were larger in Caucasians as compared to Indians, but no difference after correction for BSA.[23] Our QCA findings are comparable and substantiated by a study in similar population contradicting the traditional belief of Indians having smaller coronaries.[24] The vessel diameters in this study by IVUS were significantly larger than dimensions obtained by QCA.

Previous studies from Indian subcontinent by QCA found that males had statistical significant larger coronary artery diameters as compared to females but there was no difference after indexing to BSA.[23,25] However, Elangovan et al found small coronary size in females after correction for BSA.[26] Autopsy series data in humans found smaller coronary artery size in females.[27] In patients undergoing CABG, females had smaller coronary artery diameter and was associated with increased mortality.[28] In the present study by IVUS, males had larger coronary artery dimensions as compared to females but after indexing to BSA there was no statistical significant difference except in left circumflex artery. This finding is probably due small sample size of LCX in females. Our study negates the general belief that women have smaller coronary size.

The size of normal left main artery in present study is comparable to the western population.[29,30] The mean left main minimal luminal diameter was 4.60 ± 0.69 mm in males and 4.50 ± 0.79 mm in females, whereas in study by Kim et al.,[29] it was in males 4.26 ± 0.55 mm and in females 3.92 ± 0.45 mm. In our study, the lower limit of left main coronary diameter as per 2 SD below the mean is 3.22 mm with a 95% CI 4.52–4.68. Multiple factors affect the coronary artery size, and each systemic factor may not affect all coronary arteries in a similar way.[31–33] Kornowski et al. found no gender difference after correcting for body surface area on IVUS but the study was limited by disease vessels at multiple locations.[34] The body surface area and gender were reported to be independent predictors of left main coronary artery size.[29] Sheifer et al. observed gender difference in coronary size in LM and LAD.[35] In contrary, gender was not an independent predictor of coronary artery size in our study. However, body surface area and age were independent predictors of coronary artery size and area in LM and LAD. This could be due to the fact that LM and LAD supply large area of the myocardium. It has been known that ventricular mass strongly predicts the size of coronaries.[29,32,36,37] In the present study, hypertension independently predicted the coronary artery area in LAD. Hypertension causes left ventricular hypertrophy, which increases the myocardial mass (weight). LAD subtends the left ventricular wall, thereby causing larger diameters in this artery.

5. Study strengths and limitations

This is the first of its kind study to assess the coronary artery size by intravascular ultrasound imaging in the Indian population. All coronary artery segments were not analyzed in a single individual. The proportion of females was less.

6. Conclusions

The coronary artery dimensions as assessed by intravascular ultrasound are significantly larger than as measured by quantitative coronary angiography. Body surface area was an independent predictor of coronary artery size. Age was an independent predictor of coronary artery size and area in left main and LAD. Gender and diabetes did not influence the coronary artery size. The coronary artery size *per se* may not be a risk factor for acute coronary syndrome.

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Declaration of competing interest

All authors have none to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2019.10.005.

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