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Pitfalls in comparison of coronary artery measurements of Indian population with different geographical area studies



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ABSTRACT

Introduction: Coronary artery disease (CAD) is the most common cause of morbidity and mortality especially in the developing countries. Coronary artery measurements (CAM) are the most important factor affecting the procedure and outcome of coronary angioplasty (PCI) as well as coronary by-pass operations (CABG). In this study, we aimed to establish a database for the normal CAM as well as for gender difference among the Indian population using quantitative coronary angiography (QCA) with an objective of assessing normal coronary vessel morphology of patients with normal coronaries.

Materials and methods: Four thousand angiograms from patients of Indian origin were studied prospectively after procuring the sanction for the same from the ethical committee of the pre-selected hospitals of four states in India. Informed consents were obtained. Post CABG, post PCI patients and patient being diabetic for \geq 5 years were also excluded from the study.

Results: Ten segments from right and left coronary arteries were taken for diameter measurements. These coronary diameters were indexed to body surface area (BSA) (mean diameter mm/m² BSA). Among, 4000 patients, 933(23.3%) [M:F-521:412] had normal coronaries and 3067 (76.7%) were diseased. *Discussion and conclusion:* The dimensions of the coronary artery segments of Indians were smaller (in BSA indexed and non-indexed data), compared to studies from other continents which can be due to their smaller BSA.

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1. Introduction

Coronary artery diameter is one of the most important factors that affect the procedure and outcome of percutaneous coronary angioplasty (PCI) as well as coronary bypass operations (CABG).¹ Lumen diameter of normal human coronary arteries and several factors affecting the lumen diameters have been studied previously in different countries on different populations.^{2–7} Previous studies among Asian migrants living in western countries have pointed towards disease and diet differences among different Asian ethnicities.⁸ Studies from Asia have found that different ethnic groups within Asia like Indians and Indonesians have differences regarding the prevalence of cardiovascular risk factors.^{9,10} Studies among South Asian ethnic group in the United States, shows an increased risk for cardiovascular disease (CAD) compared to the general population.¹¹ The right (RCA) and left (LCA) coronary arteries arise from the ascending aorta from its anterior and left posterior sinuses. The level of the coronary ostium is variable.¹²

Coronary artery dimensions are known to be affected by physiological and pathological conditions; the number of published

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Abbreviations: LMCA, Left main coronary artery; LAD (OP), Left anterior descending artery (OstiumProximal part); DIAG, Diagonal; LCx (OP), Left circumflex coronary artery; OM, Obtuse Marginal; RCA (OP), Right coronary artery; RAM, Ramus; BSA, Body surface area.

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studies investigating CAM in individuals without artery diseases is very few. The clinical and therapeutic implications of a narrow or wide coronary artery are likely to affect the outcomes: both clinical and international. In this study, we aimed to establish a database for the normal CAM as well as for gender difference among the Indian population using quantitative coronary angiography (QCA) with an objective of assessing normal coronary vessel morphology of patients with normal coronaries by a multi-centre study. This helped to prove the hypothesis of pitfalls in comparison with other geographical area studies.

2. Methods

2.1. Study population

A cross sectional study was conducted in four cities of India. Hospitals were purposely selected according to the number of cardiac patients identified by them. QCA images of 4000 cases that have undergone the evaluation for CAD were included by convenience sampling technique. The sample size was estimated by consulting a statistician and using the statistical software G* Power 3.0.10. Prior ethical approval was obtained from all the study centres. A total of 3067 cases were excluded by the authors for the following reasons: presence of athermanous changes, coronary artery luminal dilatation due to various reasons, presence of coronary artery origin abnormalities, absence of the left main coronary artery (LMCA), presence of metal artifacts such as surgical clips or pacemaker leads leading to difficulty in evaluation, altered coronary anatomy due to operation as well as patients being diabetic for five or more than five years. Thus, 933 cases made up the study population (521 men and 412 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 abnormalities, a positive treadmill test or echocardiogram 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%.¹¹

2.2. Database pooling

Right and left coronary artery of normal cases with its main branches vessel morphology were measured at ostium and proximal segment by stenosis analysis programme using the automated coronary analysis package of the Innova 2100 IQ Cath at an AW4.4 workstation or Siemens QCA - Scientific coronary analysis. QCA were performed for vessel diameters ranging from 0.5 mmto 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. Calibration assessments from QCA¹⁴ systems were carried out by the same method in which the coronary catheter was employed for angiography procedure. This was used as calibrating the object by automated edge detection technique resulting in corresponding calibration factors (mm/pixel) and the vessel contour were detected by operator independent edge detection algorithms. The dimension of the coronary artery was then measured using the catheter diameter; the absolute diameter in mm was calculated by the computerized software analysis separately. 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 interobserver variability was accounted during statistical analysis. The gender wise categorisation of the data was done to denote the mean differences in the artery measurements.

LMCA, left anterior descending artery (LAD) and left circumflex artery (LCx) were assessed for LCA segment analysis. For LAD, ostial and proximal segment before the origin of the first septal branch (S₁) were measured. Measurement of the first diagonal (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 obtuse marginal (OM) for the proximal segment calibration assessment. The ostiums of the OM were calibrated for its measurement. For RCA, the ostium and proximal segments were measured before the origin of first acute marginal. The ostium of the ramus intermedius (RAM) were also calibrated for its measurement, in cases where it was detected. Angiographic views were selected for calibration assessment by minimising the foreshortening of the coronary segments by separating them from adjacent intervening structures. 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.

ii. Patient's anthropometric measurements were done using the fore mentioned relevant equipments in the methodology. BSA was calculated from patient's height and weight measurements data using Mosteller's formula.¹⁵ The diameters of the ten segments of coronary artery from angiogram study samples were indexed (adjusted) to body surface area (mean diameter mm/m²BSA) (Fig. 1).

2.3. Statistical analysis

Statistical analysis of the present study was done using the SPSS software package for Windows version 22.0 (SPSS Inc., Chicago, IL). Mean/median/mode with respective intervals were used to express coronary vessel dimensions and percentages. This helped for presenting categorical data. Coronary artery diameters were indexed (adjusted) to BSA using the formula, mean CAM in mm/BSA m² (mean diameter mm/m² BSA). Independent *t*-test, and analysis of variance (ANOVA) were used for metric data. Post-hoc tukeys test was used for multiple comparisons. Independent variables were gender and BMI and dependent variables were coronary vessel size and CAD.

3. Results

Based on QCA analysis, categorisations of 4000 samples were done. Among total sample population, there were 2696 (67.4%) males and 1304 (32.6%) females. Mean age of the patients was 54.50 ± 8.45 years (range 30–75 years). Among total sample population, normal coronary arteries were seen in 933 (23.3%) cases and 3067 (76.7%) had diseased coronary arteries. Length of LMCA was short in 225 cases. Majority of the LAD (90%) were of type III variety.

Physical and demographic parameters were assessed. The average weight was $63.19 \pm 5.09 \text{ kg}$ (range 90.00-37.00 kg), height was $168.15 \pm 4.60 \text{ cm}$ (range 190.00-135.00 cm). BMI and BSA of the normal samples were calculated. Mean body mass index (BMI) was $24.59 \pm 1.48 \text{ kg/m}^2$ (range $31.30-21.26 \text{ kg/m}^2$). Mean body surface area (BSA) was $1.75 \pm 0.11 \text{ m}^2$ (range $1.36-1.99 \text{ m}^2$).

The diameters of the 10 segments of coronary arteries of both non-indexed and indexed CAS (adjusted) to BSA (mean diameter mm/m^2 BSA) which is measured by QCA analysis programme has been assessed. Gender wise categorized samples indicated CAM



Fig. 1. Study plan-Flow chart; Abbreviations: QCA- Quantitative coronary, angiography, BMI- Body mass index, CAM- Coronary artery measurements, SVD-Single vessel disease, DVD-Double vessel disease, TVD-Triple vessel disease.

was lesser among females than males for all coronary artery segments (CAS). The differences were highly significant (p < 0.001) (Tables 1 and 2). The diameters of the normal non-indexed CAS were not measurable in certain segments due to anatomical peculiarities.

4. Discussion

The dimensions of the coronary arteries vary significantly among normal population.^{12,16} Several studies have validated the accuracy of digital quantitative estimation of coronary dimensions.^{17,18} Indians have small sized coronary artery because of their smaller body surface area. This has great relevance to the performance and results of interventional procedures like angioplasty and coronary artery bypass graft surgery. The clinical and therapeutic implications of a narrow or wide coronary artery are likely to affect the outcomes: both clinical and international. Coronary artery size in Indians has been reported to be significantly smaller compared to that of the western population.^{6,18} QCA,¹⁴ which has been developed with the purpose of geometric assessment of epicardial coronary artery abnormalities, since visual interpretations by QCA is inherently flawed and observer dependent. Several studies have validated the accuracy of digital QCA estimations for measuring the coronary dimensions.^{18,19}

In the present study, the mean diameter of left coronary system which mainly includes LMCA, LAD and LCx were 4.16 ± 0.70 mm, 3.22 ± 0.60 mm (LAD-p) and 3.02 ± 0.62 mm (LCx-p), respectively, and for the right coronary system of RCA was 3.05 ± 0.65 mm (RCA-p). As of now in India, there are no standard reference dimensions for CAM which can be used for clinical purposes. Literature search revealed only few studies that incorporated this objective done with methodological rigour, but they were done in single centres with limited sample size and similar cross section of people from a single centre. The present study had a wider age group population from varied cross-sectional areas as study samples. With, regard to indexed RCA measurements the findings of the present study was similar to that of several other studies.^{2,19}

The normal CAM of the present study was comparable to the study results of a single centre study,²⁰ even though their methodology was different. Non-indexed CAM from the studies^{2,19} had

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Measurements of the diameters of no	ormal un-indexed coronary arte	rv segments among samples	s along with gen	der comparisons ()	n = 933
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CAS	Total samples	Mean ± SD (mm) (n:933)	Male samples	Mean ± SD (mm) (n:521)	Female samples	$\begin{array}{l} \text{Mean} \pm \text{SD} \ (mm) \\ (n=412) \end{array}$	t-value	p-value
LMCA	927	4.16 ± 0.70	518	4.24 ± 0.70	409	4.07 ± 0.66	-3.876	<0.001*
LAD-o	930	3.18 ± 0.62	518	3.24 ± 0.63	412	3.10 ± 0.59	-3.692	< 0.001*
LAD-p	929	3.22 ± 0.60	520	3.29 ± 0.59	409	3.13 ± 0.58	-3.959	<0.001*
DIAG	912	1.76 ± 0.44	509	1.82 ± 0.45	403	1.69 ± 0.40	-4.765	<0.001*
LCX-o	933	3.04 ± 0.62	521	3.11 ± 0.61	412	2.97 ± 0.62	-3.459	< 0.001
LCX-p	931	3.02 ± 0.62	521	3.09 ± 0.62	410	2.94 ± 0.61	-3.732	<0.001*
OM	915	2.10 ± 0.50	513	2.13 ± 0.51	402	2.06 ± 0.49	-1.894	< 0.059
RCA-o	917	3.15 ± 0.66	508	3.24 ± 0.66	409	3.03 ± 0.65	-4.647	<0.001*
RCA-p	926	3.05 ± 0.65	515	3.14 ± 0.66	411	2.95 ± 0.62	-4.269	<0.001*
RAM	102	2.25 ± 0.49	61	2.28 ± 0.52	41	2.21 ± 0.46	-0.611	< 0.542

 $p < 0.001^*$ indicates significant difference between coronary artery measurements of males and females; Abbreviations: n-normal samples, TS-Total Samples, MS-Male samples, FS-Female samples, LMCA - Left main coronary artery, (AD (O, P) - Left anterior descending artery (Ostium, Proximal part), DIAG - Diagonal branch of left anterior descending artery, (LX (O, P) - Left circumflex coronary artery, (Ostium, Proximal part), OM - Obtuse Marginal branch of left circumflex coronary artery, RCA (O, P) - Right coronary artery (Ostium, Proximal part), RAM – Ramus branch of coronary artery. Statistical test used: Mean \pm SD, Independent-t test.

Table 2

Measurements of the diameters of normal indexed coronary artery segments among samples along with gender comparisons (n = 933).

CAS	Total samples	Mean ± SD (mm) (n:933)	Male samples	Mean ± SD (mm) (n:521)	Female samples	$\begin{array}{l} \text{Mean} \pm \text{SD} \ (mm) \\ (n = 412) \end{array}$	t-value	p-value
LMCA	927	2.46 ± 0.48	518	2.47 ± 0.49	409	2.44 ± 0.48	-0.889	0.374
LAD-o	930	1.88 ± 0.43	518	1.90 ± 0.43	412	1.86 ± 0.43	-1.124	0.261
LAD-p	929	1.90 ± 0.41	520	1.92 ± 0.40	409	1.89 ± 0.42	-1.084	0.279
DIAG	912	1.05 ± 0.28	509	1.07 ± 0.29	403	1.02 ± 0.26	-2.665	0.008
LCX-0	933	1.80 ± 0.43	521	1.82 ± 0.43	412	1.78 ± 0.43	-1.295	0.196
LCX-p	931	1.79 ± 0.42	521	1.81 ± 0.42	410	1.77 ± 0.42	-1.508	0.132
OM	915	1.24 ± 0.33	513	1.24 ± 0.33	402	1.24 ± 0.33	-0.029	0.977
RCA-o	917	1.86 ± 0.44	508	1.89 ± 0.45	409	1.83 ± 0.44	-2.061	0.040
RCA-p	926	1.81 ± 0.43	515	1.83 ± 0.44	411	1.78 ± 0.42	-1.915	0.056
RAM	102	1.35 ± 0.36	61	1.35 ± 0.38	41	1.34 ± 0.32	-0.038	0.970

Table 3

Comparison of normal	non-indexed co	ronarv arterv m	leasurement dat	ta of the present s	study with o	other studies from	South-Central Asia.
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CAS	С	Present study n = 933, M:F 521:412	Kaimkhani et al, 2004 Pakistani study n = 200	p-value	Dhakal et al, 2015 Nepali study (M:F 57:43)	p-value
LMCA	Т	4.16 ± 0.70	4.28 ± 0.77	0.03	NA	NA
LMCA	М	4.24 ± 0.70	NA	NA	4.42 ± 0.45	0.06
LMCA	F	4.07 ± 0.66	NA	NA	4.34 ± 0.54	0.01
LAD-p	Т	3.22 ± 0.60	3.22 ± 0.58	1.00	NA	NA
LAD-p	М	3.29 ± 0.59	NA	NA	3.3 ± 0.37	0.90
LAD-p	F	3.13 ± 0.58	NA	NA	3.2 ± 0.31	0.37
LCx-p	Т	3.02 ± 0.62	3.02 ± 0.62	1.00	NA	NA
LCx-p	М	3.09 ± 0.62	NA	NA	3.1 ± 0.50	0.91
LCx-p	F	2.94 ± 0.61	NA	NA	3 ± 0.47	0.53
RCA-p	Т	3.05 ± 0.65	3.08 ± 0.65	0.57	NA	NA
RCA-p	М	3.14 ± 0.66	NA	NA	3.23 ± 0.50	0.32
RCA-p	F	2.95 ± 0.62	NA	NA	3.03 ± 0.57	0.42

AbbreviationsCAS, Coronary artery segments, C, Category, LMCA, Left main coronary artery, LAD (P), Left anterior descending artery (Proximal part), DIAG, Diagonal branch of left anterior descending artery, LCX (P), Left circumflex coronary artery (Proximal part), OM, Obtuse Marginal branch of left circumflex coronary artery, RCA (P), Right coronary artery (Proximal part), T, total samples, M, Males, F, Females, NA, Not applicable.

Statistical test used: Student *t*-test, p < 0.05 indicates a statistically significant difference.

difference in the dimensions for all CAS compared to the present study (Tables 3 and 4). In both studies, the CAM normalised for BSA was calculated using Mostellar formula.¹⁵ This can be the possible reason behind the similarity with the indexed segments. Less advanced calibration analysis which was done more than a decade before by the authors² with non-indexed data must have resulted in the dissimilarity with the present study. Improved analysis techniques and software's might have contributed to the enhancement in better determination of CAM of the present study results. On the basis of this study authors suggest that indexing with the BSA may not be an accurate method of coronary dimension analysis. However, more studies are needed to determine whether CAM Indexed to BSA or non indexed CAM should be considered for clinical purposes.

The present study compared the indexed CAM with a study which incorporated the indexed CAM from a South Asian Vs Caucasian region²¹ and with a study from Indo-Asian Vs Caucasian study group of indexed and non-indexed CAM.¹⁵ When the indexed measurements of LMCA were compared with the study results of²¹ they were found similar. But, an overall decrease in the diameters of

Table 4

Comparison of normal non-indexed coronary artery measurement data with of the present study other geographical area studies.

CAS (mm)	С	Present study n = 933, M:F 521:412	Ozan et al, 2016 Turkish study n = 77, M:F 26:51	p-value	lmad et al, 2014 Iraqi-Kurdish study M:F 59:29	p-value	Felix et al, 2006 USA study M:F 55:90	p-value	Kim et al, 2005 Korean study M:F 23:53	p- value
LMCA	Т	4.16 ± 0.70	4.59 ± 0.76	<0.001*	NA	NA	NA	NA	NA	NA
LMCA	Μ	4.24 ± 0.70	4.59 ± 0.86	0.01	4.86 ± 0.77	<0.001*	4.7 ± 0.70	<0.001*	4.4 ± 0.50	0.28
LMCA	F	4.07 ± 0.66	4.35 ± 0.69	<0.001*	4.5 ± 0.73	<0.001*	4.2 ± 0.60	0.09	4.5 ± 0.60	<0.001*
LAD-p	Т	3.22 ± 0.60	3.48 ± 0.53	<0.001*	NA	NA	NA	NA	NA	NA
LAD-p	Μ	3.29 ± 0.59	3.63 ± 0.51	<0.001*	3.6 ± 0.58	<0.001*	3.7 ± 0.60	<0.001*	3.9 ± 0.40	<0.001*
LAD-p	F	3.13 ± 0.58	3.4 ± 0.52	<0.001*	3.31 ± 0.46	0.10	3.3 ± 0.50	0.01	3.6 ± 0.60	<0.001*
LCx-p	Т	3.02 ± 0.62	3.11 ± 0.67	0.22	NA	NA	NA	NA	NA	NA
LCx-p	Μ	3.09 ± 0.62	3.29 ± 0.67	0.11	3.26 ± 0.62	0.05	3.6 ± 0.60	< 0.001*	3.3 ± 0.50	0.11
LCx-p	F	2.94 ± 0.61	3.01 ± 0.66	0.44	3.03 ± 0.39	0.43	3 ± 0.50	0.38	3.1 ± 0.50	0.07
RCA-p	Т	3.05 ± 0.65	3.45 ± 0.50	<0.001*	NA	NA	NA	NA	NA	NA
RCA-p	Μ	3.14 ± 0.66	3.55 ± 0.46	<0.001*	3.26 ± 0.65	0.19	3.8 ± 0.80	< 0.001*	4.1 ± 0.40	<0.001*
RCA-p	F	2.95 ± 0.62	3.4 ± 0.52	<0.001*	3.02 ± 0.55	0.55	3.3 ± 0.60	< 0.001*	3.7 ± 0.50	<0.001*

AbbreviationsC, Category, LMCA, Left main coronary artery, LAD (P), Left anterior descending artery (Proximal part), DIAG, Diagonal branch of left anterior descending artery, LCx (P), Left circumflex coronary artery (Proximal part), OM, Obtuse Marginal branch of left circumflex coronary artery, RCA (P), Right coronary artery (Proximal part), M, Males, F, Females, NA, Not applicable.

Statistical test used: Student *t*-test, p < 0.05 and p < 0.001* indicates a statistically significant difference.

the indexed coronaries was found when compared with the present study results. The LMCA measurements of the present study were more similar to the Caucasian group than the Indo-Asian groups.⁶ Though the CAM normalised for BSA was used by both the authors, the adjustment for BSA could not wholly account for the differences in the CAM from different ethnic groups. The dissimilarity between the South Asian group and the present study results can be due to fewer samples used by the authors and the study group not being inherently homogeneous in their studies.

The non-indexed CAM of the present study had smaller diameters for all CAS than the Caucasian study group of,⁶ but, compared to Indo-Asians, they had bigger dimensions for the CAS. The difference seen with the Caucasian study may be because it incorporated samples from a different geographical area with differences in the BSA. Thus, the difference could be attributed to the difference in ethnicity. But, the sample sizes in both studies were considerably different. The other factor that may have contributed may be the accuracy of the stenosis analysis programme in their study, which was done two decades back, which may have its inherent limitation of calibration difference.

Dimensions of CAM non-indexed with BSA from a Nepali study²² and also from studies conducted in Pakistan⁴ was statistically similar to the present study results except for LMCA measurements. People from India, Pakistan, Bangladesh, Nepal, and Sri Lanka originate from a large geographic area commonly termed as South Asians/Asian Indians.²³ The similar ethnic origin and characteristics must have resulted in the similarity in the CAM. However, LMCA dimensions need to be assessed in a wide sample population for accurate comparison analysis.

The present study attempts to compare coronary artery morphology between ethnic groups to have a database for the same. Although many investigators have attempted to measure coronary artery size,^{5,24} very few have compared coronary anatomy between ethnic groups. A few segments of indexed coronaries were only statistically similar to the studies conducted at Iran and Israel respectively.^{25–27} Even the adjustment for BSA attenuated could not wholly account for difference in various ethnic groups. However, it has been postulated that the differences could be due to extreme end of population samples, i.e., all samples being underweight, all samples being big or small stature used by two different authors, samples from different geographical areas, along with differences in base line characteristics, etc.

Studies on non-indexed CAM analysis from other geographical regions of Turkey²⁸ had statistical similarity only for LCx of CAM with the present study. Iranian and Israelian regional study observations indicated that none of the coronary artery segments from the present study were statistically similar with their study [30–32]. Only, the RCA measurements of the present study were statistically similar to those of the USA, Iraqui-Kurdish and Korean region studies.^{3,16,29}

5. Conclusions

In this study, authors conclude that the CAM of the investigated population had decreased dimensions when compared to recent study data of dimensions of the coronary arteries from other continents. However, this warrants further investigation with larger multi centric study involving different ethnic groups from the country.

5.1. Limitations of the study

Decade-wise age adjusted data of coronary artery measurements would have enhanced the study results. We cannot extrapolate these results to the whole population of India as the study is not the representation of the entire population. However, this can inspire the other researches to conduct the same type of study in east, west or north Indian centres which we couldn't do.

Coronary artery diameter indexed (adjusted) to body surface area (mean diameter mm/m² BSA). $p < 0.001^*$ indicates significant difference between coronary artery measurements of males and females.; Abbreviations: n- normal samples, CAS- Coronary artery segments, LMCA - Left main coronary artery, LAD (O, P) - Left anterior descending artery (Ostium, Proximal part), DIAG - Diagonal branch of left anterior descending artery, LCx (O, P) - Left circumflex coronary artery (Ostium, Proximal part), OM - Obtuse Marginal branch of left circumflex coronary artery, RCA (O, P) -Right coronary artery (Ostium, Proximal part), RAM – Ramus branch of coronary artery. Statistical test used: Mean \pm SD, Independent-t test (p) *Body surface area* (*BSA*) =

 $\sqrt{\frac{ht \ in(\ cms) \times wt \ in \ (kgs)}{3600}}$

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