Open Access

Original Article

ADULT CARDIOLOGY

Determination of Left Main Coronary Artery Luminal Area Using CT Angiography in Individuals with Un-Obstructive Coronary Arteries

Zohair Aziz, Syed Khurram Shahzad, Fahd-Ur-Rehman, Ismail Ahmed Khan, Asma Zafar Khawaja, Hafiz Muhammad Shafique, Abdul Hameed Siddiqui, Zahoor Aslam Khan

Department of Adult Cardiology, Armed Forces Institute of Cardiology/National Institute of Heart Diseases/National University of Medical Sciences (NUMS), Rawalpindi, Pakistan

ABSTRACT

Objective: To assess the Minimal Luminal Area of the left main coronary artery in cardiac patients having un-obstructed coronary arteries.

Study Design: Analytical, cross-sectional study.

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi Pakistan, from April-Sep 2023.

Methodology: Total eighty six individuals with low risk pre-test probability for Coronary artery disease (via CAD consortium calculator) underwent a CT angiogram and their Left Main Coronary Artery Minimal Luminal Area was calculated using dedicated software over a 2-month period. Approval from the Ethical Review Board was sought. Sampling was done by using non-probability consecutive sampling. Student t-test was applied to find the mean difference of LM-MLA between factors such as diabetes mellitus, hypertension, gender, and smoking status with Minimal Luminal Area. Pearson correlation was applied to find correlation between Left Main Coronary Artery Minimal Luminal with age, BMI, BSA, and LV-mass. $p<0.05$ was taken as statistically significant.

Results: Out of total n=86 individuals, 67(77.9%) were males and 19(22.1%) were females with average age of 45.78±11.40 years. The mean Minimal Luminal Area of study sample was 12.07±4.17mm^2 with males having a mean Minimal Luminal Area of 12.79±4.31mm^2 and females having a mean MLA of 9.50±2.26mm^2. It was noted that an increased LV mass leads to an increase in LM-MLA (r=0.579, $p < 0.001$).

Conclusion: Variety of factors influence the Left Main Coronary Artery Minimal Luminal which means local guidelines would have to be set up to dictate treatment threshold in patients with Left Main Stem diseases. There is a requirement for further studies with larger sample sizes to get the average dimensions of Left Main Coronary Artery Minimal Luminal through which clinicians can establish recommendations when to intervene in patients having Left Main Stem disease.

Keywords: CT coronary angiogram, Left main coronary artery, Minimal luminal area.

How to Cite This Article: *Aziz Z, Shahzad SK, Rehman FU, Khan IA, Khawaja AZ, Shafique HM, Siddiqui AH, Khan ZA. Determination of Left Main Coronary Artery Luminal Area Using CT Angiography in Individuals with Un-Obstructive Coronary Arteries. Pak Armed Forces Med J 2024; 74(Suppl-1): S27-S31. DOI: https://doi.org/10.51253/pafmj.v74i.-SUPP-1-10637*

INTRODUCTION

Left main stem disease is associated with significant morbidity and mortality with mortality rate approaching as high as 15% as per a recent study conducted in Pakistan.[1] Despite carrying such a high morbidity and mortality in the country, left main stem disease evaluation remains a dilemma as the angiographic assessment of left main disease remains inadequate. Therefore, it is necessary to address it appropriately either via medical treatment or with invasive strategy. Current practice states the cut-off value for critical left main coronary luminal area as less than 6mm^2 necessitating invasive management either via coronary artery bypass graft or Percutaneous Coronary Intervention (PCI).[2] The European bifurcation club (EBC) has set the cut-off as being less than 6mm.[2,3] However, this cutoff carries a caveat as this is based on European population. Numerous studies have shown that the LM-MLA varies with different populations. In a study conducted in India, the MLA was calculated to be 17mm.[2,4] A study conducted by Skowronski J *et al*., compared LMCA MLA in Polish and Asians, showed that Polish had larger vessels compared to Asians.[5] Based on these numbers, it would suggest that the 6mm2 cutoff set by the EBC would not be appropriate for every individual and found to have a diseased left main coronary. Therefore, it is necessary to conduct studies based on region, so local guidelines can be set up to help solve this problem. In Pakistan, a recent study showed that around 37% of the respondents had left main stem disease thereby necessitating the need to establish local guidelines.[6]

Correspondence: Dr Zohair Aziz, Department of Adult Cardiology AFIC/NIHD, Rawalpindi, Pakistan

Traditionally, LMCA-MLA is quantified using Intravascular Ultrasound (IVUS) during a coronary angiogram, but studies have shown that CT angio-graphy can deliver comparable results to IVUS while also being non-invasive and minimizing the risk to the individual.[7]

LMCA-MLA has been noted to be influenced by a variety of factors such as diabetes, hypertension, LV mass and gender.[8] The purpose of this study was to assess the LM-MLA in a subset of patients presenting to a tertiary care hospital with suspected coronary artery disease with the goal to conduct local research on how and when to best approach left main coronary artery disease and also to assess which anthropometric parameters have an effect on the MLA if *at all*. The aim of this study was to assess the minimal luminal area (MLA) of the LMCA in cardiac patients having un-obstructed coronary arteries.

METHODOLOGY

Our study was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Disease, Rawalpindi Pakistan, from April to September 2023. It was an Analytical Cross-sectional study done after formal approval from Institutional Ethical Review Board (IERB) (Ltr# 9/2/R&D/2023/246) and there were no ethical issues. Patients were informed and consent was taken. Non-probability consecutive sampling technique was used to collect data.

Sample size of n=84 was calculated by using 5.79% prevalence of patients with atypical chest pain and normal ECG undergoing CT-angiography with normal coronaries. Confidence level of 95% and margin of error of 5% was kept.[9] However, total n=86 patients were enrolled in this study.

Inclusion criteria: Individuals enrolled in the study were those who presented to the hospital with complaints of chest pain with low probability of coronary artery disease as calculated by CAD con-sortium calculator. Patients with history of syn-cope, exertion dyspnea and abnormal ECG changes but not overtly suggestive of MI were included in the study.

Exclusion criteria: Any individual who previously had a history of coronary artery disease ,chronic kidney disease as well as those with rhe-umatic heart disease were excluded from the study.

Prior to testing the individuals, a brief clinical history was taken with emphasis on history of chest pain, shortness of breath, family history for heart disease and any co-morbidities predisposing to coronary artery disease. Total of n=303 individuals were included in the study who presented with atypical chest pain with normal ECG findings. They were under suspicion of having coronary artery disease so proceeded for CT-angiography. The patient's height and weight were documented prior to CT Angio from which BMI and body surface area were calculated.

2D-echocardiography was done in the enrolled respondents to evaluate ejection fraction, LV mass, and exclude any valvular diseases. CT-angio-graphy of 217 patients showed coronary artery disease and were excluded from the study sample. While n=86 individuals were enrolled in study who had a low to moderate probability of having coronary artery disease as designated by CAD consortium score calculator. A 64-slice scanner was used to assess the Cross-sectional luminal area of the left main coronary artery. Prior to the procedure, if the heart rate of the subject was greater than 70/beats per minute then a beta blocker was given to control the heart rate. For cardiac imaging, an inspiratory breath hold was performed and 80mL of iodinated non-ionic contrast agent injection was administered at 5mL/second followed by a saline flush. The MLA was measured using dedicated software. The luminal area was measured manually from images perpendicular to the arterial axis.[10] 2D echocardiography was used to assess LV mass in all participants of the study. The LV mass was calculated using the Devereux formula[11] which is as follows:

$$0.8\{1.04[(LVEDD + IVSd + PWd]3 - LVEDD3)]\} + 0.6$$

LVEDD: Left ventricular End-diastolic Dimension; IVSd: Inter-ventricular Septal Thickness at End-diastole; PWd: Posterior Wall thickness at end-diastole.

Minimal luminal area (MLA) was defined as the smallest area through the center point of the lumen[12], and left main minimal luminal area referred to the luminal area of the left main coronary artery,[6] The LMCA arises from the mid-portion of the superior margin of the left aortic sinus of Valsalva. Typically, it runs leftward, superior, and anterior. It consists of three portions: the ostium, the portion of the left main arising from the aorta; the shaft or mid-portion; and the distal segment. It ends by bifurcating into the left anterior descending and circumflex artery. In 30% of cases, it may also give rise to a ramus intermedius vessel,[13] un-obstructive coronary artery refers to an artery with 0% visible stenosis as per the SCCT guidelines,[14] and Cardiac computed tomography (CT) is a radiographic test that allows visualization of the heart as a whole and individualized cardiac structures.[15]

Data analysis was done on Statistical Package for Social Sciences (SPSS) version 29:00. Quantitative variables were expressed as mean and standard deviations. Qualitative variables were expressed as percentages and frequencies. Student t-test was applied to find the mean difference of LMCA-MLA between factors such as diabetes mellitus, hypertension, gender, and smoking status. Pearson correlation was applied to find association between MLA and age, BMI, BSA, LV mass. *p*-value <0.05 was considered as statistically significant

RESULTS

Total (n=86) patients were enrolled in this study. The average age of the sample was 45.78±11.40 years with 67(77.9%) male patients and 19(22.1%) female patients. 34(39.5%) patients were diabetic and 16 (18.6%) were hypertensive. The mean LV mass of the sample group was 174.97 ± 39.93g with males having a greater LV mass (193.5± 16.17g) than females (109.47 ± 27.55g). The mean body surface area was 1.79±0.13 m². Also, patients who had valvular heart disease were excluded from the study as these would have changed the LV mass and therefore, would have confounded the results of the study. General characteristics of the study sample are shown in Table-I.

Table-I: Demographics, Comorbids and LV Dimensions of Study Sample (n=86)

Variables		Mean±SD/Frequency (%)
Age (years)		45.78±11.40
Gender	Male	67(77.9)
	Female	19(22.1)
BMI (kg/m²)		26.79±4.17
Body surface area (m²)		1.79±0.13
Comorbids	Diabetes Mellitus	34(39.5)
	Hypertension	16(18.6)
	Smokers	27(31.4)
LV Dimensions	LV mass in males (g)	193.55±16.17
	LV mass in females (g)	109.47±27.55
	Mean MLA (mm²)	12.07+4.17

Table-II showed the mean LMCA-MLA was found to be 12.07±4.17mm² with males having a mean MLA of 12.79±4.31mm² and females having a mean MLA of 9.50±2.26mm². The median MLA was found to be 11.90mm². Table-II showed the association of MLA with comorbids hypertension, smoking status, diabetes, and gender.A significant association was found between MLA with diabetes and gender (*p*<0.001). No significant mean difference of MLA with HTN (*p*=0.35) and smoking status (*p*=0.13) was observed.

Table-II: Association of MLA with gender and comorbids (n=86)

Variables			*p*-value
Minimal luminal area (mm²) (Mean±SD)	**Male**	**Female**	<0.001
	12.79±4.31	9.50±2.26	
Minimal luminal area (mm²) (Mean±SD)	**Diabetic**	**Non-Diabetic**	<0.001
	15.13±4.18	10.06±2.71	
Minimal luminal area (mm²) (Mean±SD)	**Hypertensive**	**Non-Hypertensive**	0.35
	11.18±3.63	12.27±4.28	
Minimal luminal area (mm²) (Mean±SD)	**Smoker**	**Non-Smoker**	0.13
	13.06±4.22	11.61±4.10	

Table-III depicted moderate and statistically significant relationship between LV mass and MLA (r=0.579; *p*<0.001). No significant correlation was found between MLA with parameters such as age, body mass index (BMI), body surface area (BSA). Also noted in diabetics was an increase in LV mass (r=0.485, *p*<0.001).

Table-III: Correlation Analysis Between MLA and Demographics (n=86)

Pearson Correlation	Age	BMI	BSA	LV mass (grams)
Correlation coefficient (r)	-0.007	-0.143	0.102	0.579
p-value	0.948	0.189	0.349	<0.001

DISCUSSION

The study showed that the LMCA-MLA was dependent on anthropometric parameters and LV structure. From the study, it was seen that LV mass was related to LMCA MLA. Diabetics also had a higher MLA than non-diabetics, however, this may be due to an associated higher LV mass. Also seen was that the MLA in males was greater than in females which may be due to a greater LV mass being seen in males. It was seen that LM- MLA is influenced by a variety of different factors such as LV mass[16], gender[17], BSA[18]. As per the guidelines a LM-MLA of less than 6mm^2 is an indication for invasive management. However, this cut-off is based on European population and not applicable to other populations where the MLA may be different. Therefore, a baseline luminal area needs to be assessed before cut-offs can be set for any given population to facilitate intervention. From the study, it can be seen that the MLA in our population varies from individual to individual (range of MLA in this study being 5.7-25.5mm^2) thus a single cut-off for MLA signifying significant LM disease may be troublesome.

Routinely LM-MLA is usually calculated via IVUS to determine the severity of the lesion and dictate further treatment plan. In this study, we preferred CT angiography as the patients tested had a low probability of having coronary artery disease and also for patient safety with CT angiography being a less invasive test and therefore, lesser risk of complications being encountered. Studies have shown that LM-MLA estimation via CT angiography is comparable to IVUS7 so in the given scenario, CT angio seemed the most appropriate investigative tool.

Patients enrolled in this study were those who had no evidence of valvular heart disease which may have led to an increased LV mass and therefore altered the results.

The average MLA of the Left Main Stem (LMS) from this study was found to be 12.07±4.17 mm^2 with males having a slightly larger mean MLA (12.79±4.31mm^2) than females (9.50±2.26 mm^2). This difference was comparable with another study where mean MLA was measured for the left main stem in normal population which averaged 16.2mm^2 for males and 14.1mm^2 for females[19], the difference accounting possibly for the different demographic in which the study was conducted. A similar study was conducted in India where the mean MLA was calculated to be 17mm^2 whereas in Poland[5], a study showed the mean MLA to be 21mm^2 and 16.8mm^2 in an Asian population. All these studies showed that the left main coronary artery MLA is not a static value and has interethnic variation highlighting all the more reason to conduct regional studies and setup guidelines tailor made for that demography for appropriate management of disease involving the left main stem.

LIMITATIONS OF STUDY

The study was conducted at a single center therefore the results cannot be considered representative of the entire population. Also, the sample size taken was not large enough. A larger sample group would help improve accuracy and more clearly reflect the MLA of the population and also better show better correlations between MLA and anthropometric parameters. Only a small number of the study group was female so the MLA recorded may not accurately reflect the actual MLA of the local female population, a bigger sample size would help rectify this concern. Coronary artery disease has a high disease burden in Pakistan.[20,21] Although there has been an increase in the number of health care facilities catering for coronary artery disease, there still remains room for improvement. Due to the large disease burden, a significant number of patients will inevitably present with disease involving the left main stem for which we have no local guidelines as to what is the target cut-off for and when to intervene.

CONCLUSION

We concluded that a variety of factors influence the LMCA-LMA which means local guidelines would have to be set up to dictate treatment threshold in patients with Left Main Stem diseases. There is a requirement for further studies with larger sample sizes to get the average dimensions of LMCA-MLA through which clinicians can establish recommendations when to intervene in patients having Left Main Stem disease.

ACKNOWLEDGEMENT

I am deeply grateful to my supervisor for his guidance, patience and support who provided insight and expertise that greatly assisted my research project. I also want to share my gratitude for Comdt AFIC/NIHD & R&D department for their support and contribution in completion of the research paper.

Conflict of Interest: Nil

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

ZA & SKS: Concept, critical review, drafting the manuscript, approval of the final version to be published

FUR & IAK: Data analysis, data interpretation, critical review, approval of the final version to be published

AZK & HMS: Study design, data acquisition, approval of the final version to be published

AHS & ZAK: Concept, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Faisal AW, Shahid NA, Habib G, Latif W, Khan SA. The Mortality in Left Main Stem Disease; A single-centre study from Pakistan. The Journal of Cardiovascular Diseases. 2021 Dec 31; 17(4).
2. Athappan G, Patvardhan E, Tuzcu ME, Ellis S, Whitlow P, Kapadia SR. Left main coronary artery stenosis: a meta-analysis of drug-eluting stents versus coronary artery bypass grafting. JACC Cardiovasc Interv. 2013; 6: 1219-1230. https://doi.org/10.1016/j.jcin.2013.07.008
3. Mintz GS, Lefèvre T, Lassen JF, Testa L, Pan M, Singh J,et al. Intravascular ultrasound in the evaluation and treatment of left main coronary artery disease: a consensus statement from the European Bifurcation Club. EuroIntervention. 2018 Jul 20; 14(4): e467-74. https://doi.org/10.4244/10.4244/EIJ-D-18-00194
4. Punamiya K, Jha T, Punamiya V, Pradham J. IVUS determination of normal left main stem artery size and plaque burden, and correlation with body surface area in an Indian population. AsiaIntervention. 2022; 8(2): 116-22. https://doi.org/10.4244/AIJ-D-22-00041
5. Skowronski J, Cho I, Mintz GS, Wolny R, Opolski MP, Cha MJ, et al. Inter-ethnic differences in normal coronary anatomy between Caucasian (Polish) and Asian (Korean) populations. European J Radiol 2020; 130: 109185. https://doi.org/10.1016/j.ejrad.2020.109185
6. Hashmi KA, Khan MR, Hashmi AA, Adnan F, Irfan M. Left main stem disease on coronary angiography in patients with non-st segment elevation myocardial infarction. Pakistan Heart Journal. 2021 May 26; 54(1): 30-3.
7. Fischer C, Hulten E, Belur P, Smith R. Coronary CT angiography versus intravasvular ultrasound for estimation of coronary artery stenosis and atherosclerotic plaque burden: a meta-analysis. J Cardiovasc Comput Tomogr. 2013; 7: 256-266 https://doi.org/10.1016/j.jcct.2013.08.006
8. Konstantinos Dean Boudoulas MD, Bittenbender PM, Nagaraja HN, Omar Kahaly MD, Dickerson JA, Raman SV, et al. Factors Determining Left Main Coronary Artery Luminal Area. Journal of Invasive Cardiology. 2017 Feb 15; 29(7).
9. Probst S, Seitz A, Martínez Pereyra V, Hubert A, Becker A, Storm K, et al., Safety assessment and results of coronary spasm provocation testing in patients with myocardial infarction with unobstructed coronary arteries compared to patients with stable angina and unobstructed coronary arteries. European Heart Journal Acute Cardiovascular Care. 2021; 10(4): 380-7.
10. Bittencourt MS, Hulten E, Polonsky TS, Hoffman U, Nasir K, Abbara S, et al. European Society of Cardiology–recommended coronary artery disease consortium pretest probability scores more accurately predict obstructive coronary disease and cardiovascular events than the Diamond and Forrester Score: the Partners Registry. Circulation 2016; 134(3): 201-11. https://doi.org/10.1161/CIRCULATIONAHA.116.023396
11. Veselka J, Cadova P, Tomasov P, Theodor A, Zemanek D. Dual-source CT angiography for detection and quantification of in-stent restenosis in the left main coronary artery: comparison with intracoronary ultrasound and coronary angiography. J Invasive Cardiol 2011 Oct 25; 23(11).
12. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. The American journal of cardiology. 1986 Feb 15; 57(6): 450-8. https://doi.org/10.1016/0002-9149(86)90771-X
13. Gao XF, Wang ZM, Wang F, Gu Y, Ge Z, Kong XQet al. Intravascular ultrasound guidance reduces cardiac death and coronary revascularization in patients undergoing drug-eluting stent implantation: results from a meta-analysis of 9 randomized trials and 4724 patients. The International Journal of Cardiovascular Imaging. 2019 Feb 15; 35: 239-47. https://doi.org/10.1007/s10554-019-01555-3
14. El-Menyar AA, Al Suwaidi J, Holmes Jr DR. Left main coronary artery stenosis: state-of-the-art. Current problems in cardiology. 2007 Mar 1; 32(3): 103-93. https://doi.org/10.1016/j.cpcardiol.2006.12.002
15. Cury RC, Leipsic J, Abbara S, Achenbach S, Berman D, Bittencourt M, et al. CAD-RADS™ 2.0–2022 Coronary Artery Disease-Reporting and Data System: An Expert Consensus Document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the American College of Radiology (ACR), and the North America Society of Cardiovascular Imaging (NASCI). Cardiovascular Imaging. 2022 Nov 1; 15(11): 1974-2001. https://doi.org/10.1016/j.jcmg.2022.07.002
16. Ramjattan NA, Lala V, Kousa O, Makaryus AN. Coronary CT angiography. 2022
17. O'Keefe JH, Owen RM, Bove AA. Influence of left ventricular mass on coronary artery cross-sectional area. Am J Cardiol. 1987; 59: 1395-1397. https://doi.org/10.1016/0002-9149(87)90927-1
18. Kim SG, Apple S, Mintz GS, McMillan T, Caños DA, Maehara A, et al. The importance of gender on coronary artery size: In-vivo assessment by intravascular ultrasound. Clinical cardiology. 2004; 27(5): 291-4. https://doi.org/10.1002/clc.4960270511
19. Litovsky SH, Farb A, Burke AP, Rabin IY, Herderick EE, Cornhill JF, et al. Effect of age, race, body surface area, heart weight and atherosclerosis on coronary artery dimensions in young males. Atherosclerosis. 1996; 123(1-2): 243-50. https://doi.org/10.1016/0021-9150(96)05815-7
20. Chatterjee A, Leesar MA, Hillegass WB. Intravascular ultrasound of normal left main arteries: Insights for stent optimization and standardization. Catheterization and Cardiovascular Interventions: Official J Society Cardiac Angiography & Interven 2019; 93(2): 239-40. https://doi.org/10.1002/ccd.28077
21. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. American heart journal. 2005 Aug 1; 150(2): 221-6. https://doi.org/10.1016/j.ahj.2004.09.025

....