Multislice CT angiography assessment of left coronary artery: correlation between bifurcation angle, dimensions and development of coronary artery disease

Abstract

Purpose: To investigate the relationship between left coronary bifurcation and dimensional changes and development of coronary artery disease using multislice CT angiography.

Materials and Methods: 30 patients (18 men, 12 women, mean age, 56 years ± 8) suspected of coronary artery disease undergoing 64- and 256-slice CT angiography were included in the study. Left bifurcation angle and left coronary diameter were measured to determine the relationship between angulation and plaque formation and subsequent dimensional changes.

Results: Plaques were present in the left coronary artery in 22 patients with variable angulations and dimensional changes. The mean bifurcation angle between left anterior descending and left circumflex arteries was measured 89.1° ± 13.1° (range, 55.3°, 134.5°) among all patients. The mean bifurcation angle measured in patients with normal and diseased left coronary artery was 75.5° ± 19.8° (range, 60°, 96.1°), and 94° ± 19.7° (range, 55.3°, 134.5°), respectively, with significant difference between these two groups (p=0.02). Similarly, there is a significant difference in the mean diameters of left anterior descending and circumflex between patients with normal and diseased left coronary artery (p<0.001), which were measured 2.8 ± 0.3 mm (range, 2.2, 3.2 mm) and 2.1 ± 0.4 mm (range, 1.9, 2.9 mm) for the normal left coronary arteries, 4.0 ± 0.8 mm (range, 2.5, 6.1 mm) and 2.9 ± 0.5 mm (range, 1.6, 3.9 mm) for the diseased left coronary arteries, respectively.

Conclusion: There is a direct correlation between left bifurcation angle and dimensional changes and formation of plaques. Multislice CT angiography can be used to provide relevant features of left coronary atherosclerosis.

Keywords: Atherosclerosis, bifurcation, coronary artery disease, left coronary artery, multislice computed tomography.

Introduction

During the past few years multislice CT (MSCT) angiography has been widely recognised as the most effective less invasive modality for diagnosis of coronary artery disease (CAD) due to its improved spatial and temporal resolution (1-3). In addition to direct assessment of coronary stenoses, MSCT allows visualization of atherosclerotic plaques (4-6). This is represented in its ability to identify the location and distribution of plaques in the coronary arteries (5, 6), characterize the type of plaques as well as assess the plaque composition (4). Recent studies have demonstrated the feasibility of differentiation between calcified, non-calcified or mixed plaques based on differences in CT attenuation (4, 7). Since the non-invasive MSCT angiography is continuously expanding, the technique will increasingly be used to identify patients at either low- or high- risk for developing coronary events, based on the composition and distribution of plaques (7).

The angulation of the left bifurcation might have an effect on shear stress and consequently on plaque size (4). Wider bifurcation angle has been reported to be related to higher turbulence and low shear stress which might induce plaque proliferation at the bifurcated regions (8-10). Studies with use of intravascular ultrasound have shown that plaque rarely occurs in the left main branch, but is much more common in the proximal segments of left coronary artery, particularly the left anterior descending artery (11, 12). Despite these reports by intravascular ultrasound, the potential impact of the left bifurcation angulation can only be investigated *in vivo* by means of non-invasive imaging techniques that provide a 3D reconstruction of the bifurcation. Multislice CT coronary angiography fulfils this goal. The purpose of this study was to correlate the left bifurcation angle with plaque formation and coronary diameters in a group of patients using multislice CT angiography. The study was conducted to explore the differences in plaque burden at the left coronary artery and its relationship of the degree of bifurcation angle and subsequent coronary dimensional changes.

Materials and Methods

Patient data and multislice CT angiography protocol

30 patients (18 men, 12 women, mean age, 56 years $\pm$ 8) suspected of CAD undergoing multislice CT examinations were included in the study. Multislice CT angiography scans were performed with a 64-slice scanner (GE Medical Systems, Lightspeed VCT, GE Healthcare, Milwaukee, WI, USA) in 20 patients and 256-slice scanner (Brilliance iCT, Philips Healthcare, Cleveland, OH, USA) in the remaining 10 patients. The scanning protocols for 64-slice and 256-slice CT angiography are as follows: beam collimation 64x0.625 mm, pitch 0.2-0.26, reconstruction interval of 0.4 mm, with tube voltage of 120 kVp and tube current modulation ranging from 300 to 650 mAs; 256x0.625 mm, pitch 0.2, reconstruction interval of 0.4 mm, with tube voltage of 120 kVp and tube current modulation of 500 mAs. Non-ionic contrast medium (Iopamiro 370 or Visipaque 320, 60-80ml) was injected onto the ante-cubital vein at 3-5ml/s for the first 40-60 ml, and 3-3.5 ml/s for the remaining 20 ml followed by 50 ml of saline chasing at 4-5 ml/s, and the scan was performed with a bolus tracking technique with a CT attenuation of 200-220 HU as the triggering threshold at the ascending aorta to initiate the scan.

Axial images were reconstructed with a slice thickness of 0.625 mm in 0.4 mm increment resulting in isotropic volume data with a voxel size of either 0.6 x 0.6 x 0.6 or 0.67 x 0.67 x 0.67 mm^3. Retrospective electrocardiographic-gating protocol was used to acquire the volume data achieving a temporal resolution of 135-165 ms in the centre of the gantry rotation. Volume data were reconstructed at 70-80% RR interval to minimize the artifacts. For patients with a heart rate more than 70 beats per minute, a beta-blocker was used to slow down the heart rate prior to CT scans.

Characterization of plaques

Original DICOM data (digital imaging and communication in medicine) were transferred to a workstation equipped with Analyze V 7.0 (AnalyzeDirect, Inc., Lexana, KS, USA) for generation of 2D and 3D reconstructed images. Coronary artery plaque was characterized into the following three types based on the CT attenuation (13): calcified plaques indicate plaques with high density (Fig 1); non-calcified plaques refer to plaques having lower density compared with the contrast-enhanced vessel lumen (Fig 2); mixed plaques indicate plaques with non-calcified and calcified elements within a single plaque (Fig 3) or within a segment of the coronary artery (Fig 4).

Measurement of left bifurcation angle and left coronary diameters

3D volume rendering and curved planar reformatted images were generated for the assessment of each bifurcation angle between the left anterior descending (LAD) and left circumflex (LCx) (Fig 5).

Since most of the coronary plaques were noticed to involve LAD and LCx, diameters of LAD and LCx were measured and compared on 2D axial images in each patient. Maximal diameters of LAD and LCx were measured with measurements repeated 3 times at each anatomic location, and the average values were used to avoid intra-observer disagreement.

Statistical analysis

All variables are expressed as mean value ± SD. Statistical tests were performed using SPSS V 17.0 (SPSS, Inc., Chicago, ILL). Comparisons were performed using one sample T test. A p value less than 0.05 was defined as statistically significant difference.

Results

The table shows the distribution and characteristics of plaques in the coronary artery and its branches. Coronary plaques were presented in 22 patients involving different artery branches, while in the remaining eight patients, the coronary artery tree was normal and free of involvement by plaques. All of the plaques have calcium components to variable degrees with more than 90% involving the left anterior descending artery.

The mean bifurcation angle (LAD-LCx) was measured 89.1° ± 13.1° (range, 55.3°, 134.5°) among all the patients. The mean bifurcation angle in patients with the normal left coronary artery was measured 75.5° ± 19.8° (range, 60°, 96.1°), and this is significantly smaller than that measured in patients with the diseased LAD (p=0.02), which was 94° ± 19.7° (range, 55.3°, 134.5°) (Fig 6). Of 22 patients with LAD disease, 15 (68%) had a bifurcation angle >80°, and 89% of the patients with both LAD and LCx disease had a bifurcation angle >90° (table).

The mean diameters of LAD and LCx among all the patients were measured 3.7 ± 0.9 mm (range, 2.2 mm, 6.1 mm) and 2.8 ± 0.6 mm (range, 1.6 mm, 3.9 mm), respectively. The mean diameters of LAD and LCx measured in patients with the normal left coronary artery were 2.8 ± 0.3 (range, 2.2 mm, 3.2 mm) and 2.1 ± 0.4 mm (range, 1.9 mm, 2.9 mm), and this is significantly smaller than those measured in patients with the diseased LAD and LCx (p<0.001) (Fig 7), which were 4.0 ± 0.8 mm (range, 2.5 mm, 6.1 mm) and 2.9 ± 0.5 mm (range, 1.6 mm, 3.9 mm), respectively.

A bifurcation angle of 80° was used as a cut-off value to categorise the extent of left coronary artery disease. The mean diameters of LAD and LCx in patients with left coronary artery disease with >80° bifurcation angle were measured 4.2 ± 0.9 mm (range, 2.8 mm, 6.1 mm) and 3.1 ± 0.4 mm (range, 2.4 mm, 3.9 mm). In contrast, the mean diameters of LAD and LCx in patients with left coronary disease with <80° bifurcation angle were measured 3.8 ± 0.5 mm (range, 3.0 mm, 4.5 mm) and 2.5 ± 0.6 mm (range, 1.6 mm, 2.9 mm), respectively. There is no significant difference in the mean LAD diameter measured between these groups of patients (p=0.32), however, the mean LCx diameter measured in patients with a bifurcation angle of >80° was significantly larger than that measured in patients with <80° bifurcation angle (p=0.04).

Since non-calcified plaques were presented in only two patients, a comparison could not be performed to determine the difference between calcified and non-calcified plaques with regard to the relationship of bifurcation angle due to a limited sample size.

Discussion

This study was performed to explore the relationship between left bifurcation angle and presence of plaques, as well as the coronary dimensional changes. Although based on a small number of patients, our study provides insights into the direct connection between bifurcation angulation and development of coronary artery disease. In addition, our results showed that the left coronary artery undergoes dimensional changes due to atherosclerosis, which is represented by the increased diameters when compared to the normal coronary artery.

It is widely acknowledged that unstable (or vulnerable) coronary plaques play a pivotal role in the pathogenesis of acute coronary syndromes due to local thrombus formation caused by plaque rupture or erosion. Therefore, plaque composition rather than the degree of luminal narrowing may be predictive of the patient's risk for further coronary events (7). Extensively calcified lesions most likely represent atherosclerosis at later stages of remodeling and may reflect more stable lesions (12). Therefore, in the presence of coronary plaques, especially calcified plaques, coronary artery undergoes dimensional changes due to remodeling process, resulting in corresponding diameter differences between the normal and diseased coronary arteries. Cademartiri et al (14) correlated the presence of atherosclerosis in the left main branch with vessel dimensional changes in terms of length and diameter using 64-slice CT. Their results demonstrated that the increase in left main branch diameters was associated with the presence of atherosclerosis, with significantly increased diameters measured at the left coronary ostium and bifurcation in patients with atherosclerotic plaques. Data from our study are in line with the literature: the mean diameter of LAD and LCx was significantly larger than that measured in the normal coronary artery, indicating the direct relationship between presence of plaques and coronary changes.

Results from this study are consistent with other reports regarding the distribution and morphology of coronary plaques (4, 8-10, 15). Atherosclerotic plaques were commonly located at the LAD, particularly close to the ostium of LAD, whereas the left main stem and the LCx were less frequently affected. This could be used as guidance for analysis of potential effects of the hemodynamics on the local characteristics and distribution of plaques (9, 10, 14), although further studies are warranted to evaluate the potential value of these findings. A comparative study of left bifurcation angle and subsequent hemodynamic changes is currently under investigation.

A bifurcation angle of 80° is recommended as a cut off value to determine whether there is presence of coronary artery disease, as this was confirmed by previous reports studying the natural distribution of coronary bifurcation angles (16, 17). In a study based on autopsies of 100 human hearts, Reig and Petit reported an average angle of $86.7^{\circ} \pm 28.8^{\circ}$ for the bifurcation angle between LAD and LCx (16). Similarly, Pflederer et al found an average bifurcation angle of $80^{\circ} \pm 27^{\circ}$ in 100 patients with suspected CAD (17), and Kawasaki et al reported the LAD and LCx bifurcation angle to be $72^{\circ} \pm 22^{\circ}$ in 209 patients (18). Our measured value correlates well with the average bifurcation angle reported by these studies. This suggests that multislice CT allows for the accurate measurements of coronary bifurcation angles, thus, the measurements can be used to determine the degree of coronary artery disease or possibility of developing atherosclerosis.

Another application of measurement of left bifurcation angle by multislice CT is to plan coronary stenting. Coronary stenting, particularly the introduction of drug-eluting stents has been increasingly used to treat coronary artery disease (19-21). The relatively low rates of in-stent restenosis have enabled the coronary stenting as an effective alternative to angioplasty with stening of the left main coronary artery (22). The description of the progression of atherosclerosis in the left coronary artery and at the bifurcation is therefore of paramount importance in the planning of stent deployment so that precise information about the type of stent to be used can be provided to ensure the success rate. Information about the coronary bifurcation angle is believed to contribute to optimize procedures and devices for stent implantation, thus potentially improve the outcome of interventional treatment of bifurcated lesions

(17). A bifurcation lesion with an angle close to 90° might be treated successfully by using the T-stenting technique to allow optimal coverage of the left side branch ostium. Multislice CT angiography could help to identify bifurcation lesions with an angle close to 90°and assist decision as to whether T-stenting should be performed.

Several limitations exist in this study. First, no correlation with invasive coronary angiography was performed. This limitation can be compensated for by the fact that multislice CT angiography was confirmed as an accurate tool to measure coronary bifurcation angles (17). Second, only the bifurcation angle of LAD-LCx was measured, while other angles such as angles between left main branch and LCx, LAD and first diagonal branch, LCx and obtuse margin, and right coronary artery and posterior descending artery, etc, were not measured in this study. This can be explained by the fact that the bifurcation angle between LAD and LCx represents the main angulation in the left coronary artery, and any change to this angulation is most importantly related to the development of atherosclerosis. Third, dimensional changes to the left coronary artery were only evaluated at LAD and LCx, while the left main branch was not assessed. As left main branch was free of involvement in most of the cases in this group, we did not perform measurements at the left main branch as we won't expect any significant difference between the normal and diseased left main arteries. Finally, only a small number of patients were included in this study. Although bifurcation angles with healthy coronary arteries differed significantly from those with coronary artery disease, only a small number of normal cases were included in our study. Further studies based on a large cohort should be conducted.

In conclusion, our results suggest that multislice CT angiography is an accurate method to measure coronary bifurcation angles and dimensional changes. Wider bifurcation angles are closed related to the presence of plaques, thus leading to the development of coronary artery disease, with subsequent coronary diameter changes.

References

1. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of non-invasive coronary angiography using 64-slice spiral computed tomography. J Am Coll Cardiol 2005; 46: 552-557.
2. Schuijf JD, Pundziute G, Jukema JW, et al. Diagnostic accuracy of 64-slice multislice computed tomography in the non-invasive evaluation of significant coronary artery disease. Am J Cardiol 2006; 98: 145-148.
3. Rybicki F, Otero H, Steigner M, et al. Initial evaluation of coronary images from 320-detector row computed tomography. Int J Cardiovasc Imaging 2008; 24: 535-546.
4. Rodriguez-Granillo GA, Rosales MA, Degrossi E, Durbano I, Rodriguez AE. Multislice CT coronary angiography for the detection of burden, morphology and distribution of atherosclerotic plaques in the left main bifurcation. Int J Cardiovasc Imaging 2007; 23:389–392.
5. Mollet NR, Cademartiri F, van Mieghem CA, et al. High resolution spiral computed tomography angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005; 112: 2318–2323.
6. Cademartiri F, Mollet NR, Runza G, et al. Diagnostic accuracy of multislice computed tomography coronary angiography is improved at low heart rates. Int J Cardiovasc Imaging 2006; 22: 101–105.
7. Schuijf JD, Beck T, Burgstahler C, et al. Differences in plaque composition and distribution in stable coronary artery disease versus acute coronary syndromes; non-invasive evaluation with multi-slice computed tomography. Acute Card Care 2007; 9: 48–53.

8. Rodriguez-Granillo GA, Garcı´a-Garcı´a HM, Wentzel JJ, et al. Plaque composition and its relationship with acknowledged shear stress patterns in coronary arteries. J Am Coll Cardiol 2006; 47(4):884–885.
9. Kaazempur-Mofrad MR, Isasi AG, Younis HF, et al. Characterization of the atherosclerotic carotid bifurcation using MRI, finite element modeling, and histology. Ann Biomed Eng 2004; 32:932–946.
10. Kimura BJ, Russo RJ, Bhargava V, McDaniel MB, Peterson KL, DeMaria AN. Atheroma morphology and distribution in proximal left anterior descending coronary artery: in vivo observations. J Am Coll Cardiol 1996; 27:825–831.
11. von Birgelen C, Klinkhart W, Mintz GS, et al. Plaque distribution and vascular remodeling of ruptured and nonruptured coronary plaques in the same vessel: an intravascular ultrasound study in vivo. J Am Coll Cardiol 2001; 37:1864–1870.
12. Hong MK, Mintz GS, Lee CW, et al. The site of plaque rupture in native coronary arteries: a three-vessel intravascular ultrasound analysis. J Am Coll Cardiol 2005; 46:261–265.
13. Pundziute G, Schuijf J, Jukema J, et al. Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007; 49: 62-70.
14. Cademartiri F, La Grutta L, Malago R, et al. Assessment of left main coronary artery atherosclerotic burden using 64-slice CT coronary angiography: correlation between dimensions and presence of plaques. Radiol Med 2009; 113: 358-369.

15. Sun Z, Dimpudus FJ, Nugroho J, Adipranoto JD. CT virtual intravascular endoscopy assessment of coronary artery plaques: A preliminary study. Eur J Radiol 2010; 75: e112-e119.
16. Reig J, Petit M. Main trunk of the left coronary artery: anatomic study of the parameters of clinical interest. Clin Anat 2004; 17: 6-13.
17. Pflederer T, Ludwig J, Ropers D, Daniel WG, Achenbach S. Measurement of coronary artery bifurcation angles by multidetector computed tomography. Invest Radiol 2006; 41: 793-798.
18. Kawasaki T, Koga H, Serikawa T, et al. The bifurcation study using 64 multislice computed tomography. Catheter Cardiovasc Interv 2009; 73: 653-658.
19. Serruys PW, de Jaegere P, Keimeneij G, et al. Benestent Study group: A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994; 331: 489-495.
20. Fischman DL, Leon MB, Baim DS, et al. Stent Restenosis Study Investigators: A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994; 331: 496-501.
21. Holmes DR Jr, Leon MB, Moses JW, et al. Analysis of 1-year clinical outcomes in the SIRIUS trial: a randomized trial of a sirolimus-eluting stent versus a standard stent in patients at high risk for coronary restenosis. Circulation 2004; 109: 634-640.
22. Valgimigli M, van Mieghem CA, Ong AT, et al. Short- and long-term clinical outcome after drug-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: insights from the Rapamycin- Eluting and

Taxus Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and TSEARCH). Circulation 2005; 111:1383–1389.

Figure legends

Figure 1. Curved planar reformatted image acquired with multislice CT angiography demonstrates calcified plaques (arrows) at the proximal and middle segments of left anterior descending artery in a 58-year-old man presenting with the symptom of chest pain (This figure has been previously published in the *Singapore Medical Journal* [2010; 51 (4): 282-289] and is produced with the kind permission of the editor).

Figure 2. Curved planar reformatted image acquired with multislice CT angiography shows a non-calcified plaque at the mid-segment of right coronary artery in a 69-year-old man suspected of coronary artery disease (This figure has been previously published in the *Singapore Medical Journal* [2010; 51 (4): 282-289] and is produced with the kind permission of the editor).

Figure 3. 2D axial image acquired with multislice CT angiography shows a mixed type of calcified plaque at the proximal segment of right coronary artery (arrow) in a 51-year-old man with significant coronary stenosis.

Figure 4. Curved planar reformatted image acquired with multislice CT angiography shows mixed type of calcified plaques at the mid-segment of right coronary artery (arrows) in a 72-year-old woman with significant coronary stenosis (This figure has been previously published in the *Singapore Medical Journal* [2010; 51 (4): 282-289] and is produced with the kind permission of the editor).

Figure 5. The left bifurcation angle was measured 96.1° in a 49-year old man presenting with the symptom of chest pain (A). Both left anterior descending (LAD) and left circumflex (LCx) are normal on 3D volume rendering image. The left bifurcation angle was measured 113.1° in a 55-year man with significant coronary

stenosis (B). Calcified plaques presented at the LAD and LCx results in irregular lumen stenosis on 3D volume rendering visualization.

Figure 6. Coronal maximum-intensity projection (A) demonstrates calcified plaques at LAD and LCx in a 42-year old man with the symptom of atypical chest pain, and 3D volume rendering shows the bifurcation angle to be 124 ° with more than 50% stenosis in the mid-segment of LAD.

Figure 7. Measurement of the left coronary artery diameter on 2D axial image in a 52-year old man with significant coronary stenosis. LAD and LCx were measured 6.1 mm and 3.7 mm due to presence of extensively calcified plaques at both artery branches (This figure has been previously published in the *Singapore Medical Journal* [2010; 51 (4): 282-289] and is produced with the kind permission of the editor).

Figure 8. Measurement of the left coronary artery diameter on 2D axial image in a 56-year old woman with suspected coronary disease. LAD and LCx were measured 2.5 mm and 2.2 mm with no sign of abnormal lumen changes.