Carina Bifurcation Angle and Side Branch Occlusion in Coronary Bifurcation Lesions Intervention: Angiographic Lesions Characteristic Role in Determining Its Relation

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Abstract

Keywords

- ▶ Carina bifurcation angle
- ▶ coronary bifurcation lesions
- ▶ elective percutaneous coronary intervention
- ▶ side branch occlusion
- ▶ plaque shifting
- ▶ carina shifting
- ▶ atheromatous plaque

Side branch occlusion has been implicated as a complication after percutaneous coronary intervention in coronary bifurcation lesions. The role of carina bifurcation angle as one of the characteristics of the coronary bifurcation lesions in causing side branch occlusion after percutaneous coronary intervention is still debated. This study aims to assess the correlation between carina bifurcation angles as one of the characteristics of the coronary bifurcation lesions and side branch occlusion in elective percutaneous coronary intervention. This is a cross-sectional study which utilizes CAAS 5.1 software to measure carina bifurcation angle. We collected 113 lesions in 108 patients that met the inclusion criteria from January 2016 to October 2016. Side branch occlusion occurred in 15 lesions (13.3%), with median carina bifurcation angle 19.17 degrees ($p < 0.001$). Multivariate analysis showed there is a correlation between carina bifurcation angle with side branch occlusion, OR (odds ratio) 0.86 (95% CI [confidence interval]: 0.80–0.92) with ≤ 33.71 degrees cut off value. Increased risk of side branch occlusion was found in small carina bifurcation angle.

Percutaneous coronary intervention (PCI) in coronary bifurcation lesions remain challenging in interventional cardiology with risk of occlusion of the side branches of the coronary artery.¹ Incidence of side branch occlusion varies from 2.7 to 10%.^{2,3} Side branch occlusion can causes ischemia to infarction of the heart muscle.^{1,2} Plaque distribution, main vessel thrombolysis in myocardial infarction (TIMI) flow grade before stenting, preprocedural diameter stenosis of proximal segment, bifurcation angle, proximal segment of the main vessel and side branch diameter ratio, and diameter stenosis of side branch have been identified as predictors of side branch occlusion after percutaneous coronary intervention in coronary bifurcation lesions.¹ However, the effect of coronary bifurcation angle on the rate of side branch occlusion is controversial.

Currently, plaque shift and carina shift are the two major mechanism of side branch occlusion after coronary bifurcation lesions intervention.⁴ Recent studies showed that wide coronary bifurcation angle (> 70 degrees) is a predictor of

side branch occlusion after percutaneous coronary intervention due to the plaque shift mechanism.¹ However, Gil et al reported that small coronary bifurcation angle (< 40 degrees) is a predictor for the occurrence of abnormalities in the side branch, restenosis, and major cardiovascular adverse events due to carina shift mechanism.⁵

Carina bifurcation angle is a part of the coronary bifurcation angle.^{5,6} This angle permits one to predict percentage diameter stenosis and minimal lumen diameter at the side branch ostium after main vessel stenting.⁵ It is a factor that governs carina position and parent vessel flow separation between branches.⁵ Vassilev et al (2012) reported that the carina shifting is one of the mechanisms causing side branch occlusion in coronary bifurcation lesions intervention in addition to the plaque shifting causes the majority of these events.⁶ Carina shifting on intra vascular ultrasound (IVUS) examination showed in the change of distal segment volume index of bifurcation after percutaneous coronary intervention.⁷ Xu

et al stated that the carina bifurcation angle of coronary artery has relationship with distal segment volume index change after percutaneous coronary intervention. The smaller the bifurcation angle of the coronary arteries, the greater the change in blood flow ($r = 0.29, p = 0.05$).⁷ Chen et al showed that the coronary bifurcation angle below 30 degrees will cause differences in blood vessel surface pressure (Wall Shear Stress Gradient), oscillatory surface pressure (Oscillatory Shear Stress), and increases incidence of intimal hyperplasia.⁸ Considering that carina bifurcation angle is one of the characteristics of the coronary bifurcation lesions and it is important in carina shift mechanism, we would like to study correlation between carina bifurcation angles and side branch occlusion in elective percutaneous coronary bifurcation lesion intervention.

Methods

Patients

A total of 894 elective percutaneous coronary intervention procedure (144 coronary bifurcation lesions) were performed in the catheterisation laboratory of National Cardiovascular Center (NCVC) Harapan Kita, Jakarta, from January to October 2016. Procedure with side branch predilatation ($n = 23$), no optimal projections for opening of bifurcation angle (overlapping vessels) on the final angiography evaluation ($n = 4$), and side branch diameter less than 1.5 mm ($n = 4$) were excluded. Overall 108 patients (aged 57.22 ± 8.46 years) with 113 coronary bifurcation lesions were eligible for analysis.

Single stent strategy was performed in all procedure and side branch flow was evaluated after stent placement. Quantitative coronary angiography software CAAS (version 5.1, Pie Medical Imaging B.V., Maastricht, The Netherlands) processed the data. Resulting in the coronary artery distribution; location of coronary bifurcation lesions; reference diameter of the main coronary arteries of the proximal segment, distal segments, and side branches of the main coronary artery; percentage diameter stenosis from the proximal, distal, and side branch segment; diameter ratio between the proximal and side branch segment; coronary bifurcation angle and carina bifurcation angle. Type of coronary bifurcation lesions are classified by Medina classification. Flow in main vessel are classified by TIMI flow grade.

Carina Bifurcation Angle Measurement

Gil et al described carina bifurcation angle by identifying projection of the widest opening between vessels branches without any overlap between vessels. However, the projection was discarded when in doubt of the double contour. A line was traced parallel to the main vessel axis and through the apex of the flow divider (apex of carina) and a line parallel to the internal contour of the side branch was traced and crossed with the first line. The resulting angle is carina bifurcation angle.⁵

Statistical Analysis

For normally distributed continuous variables, data were expressed as means $\pm$ standard deviation. If not normally distributed, data were expressed as median and interquartile

range (IQR). Categorical variables were expressed as numbers and percentages. Chi-square tests were used to compare categorical variables. Student's *t*-test or Mann-Whitney *U* test was used to compare numerical variables between the two groups. A *p* value of < 0.05 was considered statistically significant. Kolmogorov-Smirnov test was used to assess the normality of the distribution. Linear by linear association test determine the linearity aspect of statistically significant numerical variables. Variables with correlation *p* value less than 0.25 were then included in multivariate analysis. Multiple logistic regression models with an enter method were constructed for carina bifurcation angle and independent variables to establish the correlation. All statistical analyses were performed with SPSS software (version 20, SPSS Inc., IBM, Armonk, NY).

Results

Most patients with coronary bifurcation lesions were hypertensive with ejection fraction varies from 17 to 82%. Left anterior descending artery lesions were dominant. The median (IQR) coronary bifurcation angle, and carina bifurcation angle was 63.2 degrees (range: 20.38–149.7 degrees) and 39.41 degrees (10.57–95.06 degrees), respectively. Drug eluting stents with small strut thickness ($< 100 \mu\text{m}$) were used in the PCI procedure. The demographic and angiographic characteristics are presented in ►Table 1 and ►Table 2.

Carina bifurcation angle (OR [odds ratio] = 0.86, 95% CI [confidence interval]: 0.80–0.93, $p < 0.001$), ipsilateral plaque distribution in proximal segment (OR = 6.05, 95% CI: 1.22–29.92, $p = 0.015$), presence of stenosis in proximal segment (OR = 5.30, 95% CI: 1.13–24.73, $p = 0.20$) and side branch segment (OR = 9.7, 95% CI: 2.38–34.49, $p < 0.001$) correlate with the incidence of side branch occlusion (►Table 3). The multiple logistic regression model (►Table 4) showed carina bifurcation angle increase the risk of side branch occlusion in coronary artery bifurcation lesions intervention (adjusted OR 0.86, 95% CI: 0.80–0.92, $p < 0.001$).

Table 1 Patient's characteristics

Variables	Description ($n = 108$)
Age (y)	57.22 ± 8.46
Gender: male	89 (82.4)
History of acute coronary syndrome	38 (35.2)
Ejection fraction	57% (17–82)
Body mass index (kg/m^2)	25.69 ± 4.22
Hypertension	73 (67.6)
Dyslipidaemia	50 (46.3)
Diabetes mellitus	47 (43.5)
Smoking	6 (5.6)
Family history	11 (10.2)

Table 2 Coronary artery bifurcation lesion characteristics

Variables	Description (n = 113)
Right dominant coronary distribution	103 (91.2)
Left dominant coronary distribution	10 (8.8)
Location of bifurcation coronary artery	
LM	23 (20.4)
LAD	68 (60.2)
LCX	17 (15)
RCA	5 (4.4)
Medina classification	
1,0,0	14 (12.4)
0,1,0	31 (27.4)
0,0,1	7 (6.2)
1,1,0	25 (22.1)
1,0,1	12 (10.6)
0,1,1	7 (6.2)
1,1,1	17 (15)
TIMI flow	
I	1 (0.9)
II	3 (2.7)
III	109 (96.5)
Plaque distribution on proximal segment	
Ipsilateral	41 (36.3)
Contralateral	27 (23.9)
None	45 (39.8)
Proximal segment of coronary bifurcation lesions	
Reference diameter	2.79 mm ± 0.63
Stenosis larger than 50%	67 (59.3)
Length of lesion	2.67 mm (0–15.54)
Distal segment of coronary bifurcation lesions	
Reference diameter	2.11 mm ± 0.48
Stenosis larger than 50%	82 (72.6)
Length of lesion	3.5 mm (0–20.90)
Branch segment of main coronary artery	
Reference diameter	1.85 mm (1.51–3.44)
Stenosis larger than 50%	42 (37.2)
Length of lesion	1.86 mm (0–11.8)
Coronary bifurcation angle	63.2 degrees (20.38–149.7)
Carina bifurcation angle	39.41 degrees (10.57–95.06)
Side branch occlusion	15 (13.3%)

(Continued)

Table 2 (Continued)

Variables	Description (n = 113)
Types of stent	
Sirolimus-eluting stent	14 (12.4)
Zotarolimus-eluting stent	22 (19.5)
Everolimus-eluting stent	41 (36.3)
Biolimus A9-eluting stent	36 (31.9)

Abbreviations: LAD, left anterior descending; LCX, left circumflexus; LM, left main; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction flow grade.

The receiver operating characteristic (ROC) curve (►Fig. 1) showed that the cut-off point of 33.71 degrees had good sensitivity and specificity (93 and 73%, respectively) to predict side branch occlusion, with the value of Area Under Curve 0.90 (95% CI: 0.83–0.97).

Discussion

This study demonstrated that carina bifurcation angle can be used to predict side branch occlusion. Using a cut-off point of 33.71 degrees allowed the prediction of side branch occlusion with good sensitivity and specificity.

Although several studies^{1,9} showed a large bifurcation angle is a predictor for the occurrence of acute occlusion of the coronary artery side branch, none of them were built from stable coronary artery subjects. Most of them were analyzed from stable coronary artery disease subjects and acute coronary syndrome subjects. There are differences in the pathophysiology between those two entities. Subjects with acute coronary syndrome diagnosis associated with side branch occlusion are caused by the presence of thrombus.¹⁰

Different with previous studies,^{1,9} this research used homogenous stent type and thickness. The drug eluting stents used were less than 100 µm. Muramatsu et al stated that bioresorbable vascular scaffold with strut thickness 157 µm was related to a higher incidence of postprocedural side branch occlusion compared with the everolimus-eluting stent, and this effect was more pronounced with small side branches with a reference vessel diameter < 1.5 mm.² Such small side branches are more likely to be compromised by the thicker strut of the bioresorbable vascular scaffold. Beside compromised by the thicker strut, plaque shift and carina shift might play a further role in small side branch compromise and occlusion.²

Plaque shift and carina shift are the two major mechanisms in side branch occlusion.⁴ A large atheromatous plaque around the bifurcation is associated with plaque shift (the snow plough effect) to the side branch, sometimes resulting in its occlusion.⁴ A pathological study demonstrated that atherosclerotic plaques mostly occur on the lateral wall, whereas the flow divider regions (carina) tend to be spared, which may suggest that the contribution of plaque shift has been overestimated. Instead, the carina itself can be shifted to the side branch which may be the major cause of side branch compromise.^{4,11}

Table 3 Correlation between coronary artery bifurcation lesion characteristics and side branch occlusion

Variables	Occlusion	No occlusion	p-Value	OR	95% CI
Carina bifurcation angle	19.17 degrees (10.57–40.15 degrees)	41.96 degrees (12.16–95.06 degrees)	< 0.001	0.86	0.80–0.93
Plaque distribution on the proximal segment					
Ipsilateral	9 (22.0%)	32 (78.0%)	0.015	6.05	1.22–29.92
Contralateral	4 (14.8%)	23 (85.2%)	0.188	3.74	0.63–21.98
None	2 (4.4%)	43 (95.6%)			
TIMI flow					
I	0 (0)	1 (100%)	1.000	–	–
II	1 (33.3%)	2 (66.7%)	0.353	3.39	0.29–39.92
III	14 (12.8%)	95 (87.2%)			
Stenosis on the proximal segment					
≥ 50%	13 (19.4%)	54 (80.6%)	0.20	5.30	1.13–24.73
< 50%	2 (4.3%)	44 (30.7%)			
Ratio of diameter MV/SB					
≥ 1.22	8 (13.6%)	51 (86.4%)	0.926	1.05	0.35–3.13
< 1.22	7 (13%)	44 (95.7%)			
SB stenosis					
≥ 50%	12 (28.6%)	30 (71.4%)	< 0.001	9.7	2.38–34.49
< 50%	3 (4.2%)	68 (95.8%)			

Abbreviations: CI, confidence interval; MV, proximal segment of the main vessel; OR, odds ratio; SB, side branch; TIMI, thrombolysis in myocardial infarction flow grade.

Table 4 Correlation between carina bifurcation angle and side branch occlusion (adjusted)

Variables	Occlusion	No occlusion	Adjusted		
			p-Value	OR	95% CI
Carina bifurcation angle of coronary artery	19.17 degrees (10.57–40.15 degrees)	41.96 degrees (12.16–95.06 degrees)	$p < 0.001$	0.86	0.80–0.92

Abbreviations: CI, confidence interval; OR, odds ratio.

Fig. 1 Receiver operating characteristic curve.

Stent implantation on the proximal to distal segment will cause an anatomy forming the angulation to be straight (pre 148 ± 19 degrees vs. 156 ± 16 degrees after stenting, $p = 0.007$).¹² Koo et al using IVUS described that the changes of volume index in distal were not followed by the change of plaque index before and after stent implantation in coronary bifurcation lesions ($5.4 \text{ mm}^3/\text{mm} \pm 1.8$ vs. $5.3 \text{ mm}^3/\text{mm} \pm 1.7$, $p = 0.027$).¹³ Medina et al reported that an acute angulation morphology of carina (eyebrow sign) on IVUS examination is a predictor of decreased blood flow to the side branch (18 vs 1%, $p < 0.01$).¹⁴ Xu et al found that the changes in blood volume associated with the shifting of carina can cause the flow changes in the side branch ($r = 0.94$, $p < 0.001$).⁷

Different with previous studies, this study finds that ratio of diameter between proximal segment of the main vessel and side branch segment has no effect on the occurrence of side branch occlusion.⁹ Gil et al stated that the greater ratio of diameter between proximal segment of the main vessel and side branch segment, the greater coronary bifurcation angle. The risk of side branch occlusion is decreased in a wider angle.⁵

As also seen in this study, ipsilateral plaque distribution in the proximal segment of the coronary bifurcation lesions, and proximal and side branch segment stenosis are predictors in side branch occlusion after coronary bifurcation lesions intervention. Plaque displacement to the side branch occur because of plaque shift mechanism after coronary bifurcation lesions intervention.^{4,15,16} Coronary multislice computer tomography (MSCT) imaging study revealed that the thickness of plaque found on ipsilateral to the proximal segment is the cause of the occlusion on the side branch ($2.29 \text{ mm} \pm 1.87$ vs. $1.29 \text{ mm} \pm 1.43$, $p = 0.043$).¹⁵ Biore-sorbable stent implantation increase the risk of side branch occlusion in coronary bifurcation lesions intervention with proximal segment stenosis, compared with everolimus-eluting stent implantation (6.0 versus 4.1%, $p = 0.09$).² Side branch stenosis will increase the risk of side branch occlusion after coronary bifurcation lesions intervention.¹⁷ Ghayemian et al reported that stenosis in the proximal and side branch segment are the main predictors of the incidence of side branch occlusion (OR 5.91, 95% CI: 1.28–27.3, $p = 0.023$).¹⁸

Limitation

The limitation of this study is that we used two-dimensional angiography analysis to assess the coronary bifurcation lesion characteristics. Plaque and carina displacement can be measured quantitatively using three-dimensional analysis. However, two-dimensional angiography characteristics analysis may provide real world practice guidance tool in coronary bifurcation lesions intervention.

Conclusion

There is a correlation between the carina bifurcation angle and the occurrence of side branch occlusion in elective percutaneous coronary intervention. Risk of side branch occlusion increase in small carina bifurcation angle with ≤ 33.71 degrees cut-off value.

References

- Dou K, Zhang D, Xu B, et al. An angiographic tool for risk prediction of side branch occlusion in coronary bifurcation intervention: the RESOLVE score system (Risk prEdiction of Side branch Occlusion in coronary bifurcation interVention). *JACC Cardiovasc Interv* 2015;8(1, Pt A):39–46
- Muramatsu T, Onuma Y, García-García HM, et al; ABSORB-EXTEND Investigators Incidence and short-term clinical outcomes of small side branch occlusion after implantation of an everolimus-eluting bioresorbable vascular scaffold: an interim report of 435 patients in the ABSORB-EXTEND single-arm trial in comparison with an everolimus-eluting metallic stent in the SPIRIT first and II trials. *JACC Cardiovasc Interv* 2013;6(03):247–257
- Alfonso F, Hernández C, Pérez-Vizcayno MJ, et al. Fate of stent-related side branches after coronary intervention in patients with in-stent restenosis. *J Am Coll Cardiol* 2000;36(05):1549–1556
- Gwon HC, Song YB, Pan M. The story of plaque shift and carina shift. *EuroIntervention* 2015;11(Suppl V):V75–V77
- Gil RJ, Vassilev D, Formuszewicz R, Rusicka-Piekarz T, Doganov A. The carina angle-new geometrical parameter associated with periprocedural side branch compromise and the long-term results in coronary bifurcation lesions with main vessel stenting only. *J Interv Cardiol* 2009;22(06):E1–E10
- Vassilev D, Alexandrov A, Le D, et al. Importance of bifurcation angle in bifurcation stenting. *Chin Med J (Engl)* 2012;125(22):4122–4125
- Xu J, Hahn JY, Song YB, et al. Carina shift versus plaque shift for aggravation of side branch ostial stenosis in bifurcation lesions: volumetric intravascular ultrasound analysis of both branches. *Circ Cardiovasc Interv* 2012;5(05):657–662
- Chen HY, Moussa ID, Davidson C, Kassab GS. Impact of main branch stenting on endothelial shear stress: role of side branch diameter, angle and lesion. *J R Soc Interface* 2012;9(71):1187–1193
- Zhang D, Xu B, Yin D, et al. Clinical and angiographic predictors of major side branch occlusion after main vessel stenting in coronary bifurcation lesions. *Chin Med J (Engl)* 2015;128(11):1471–1478
- Popma JJ, Mauri L, O'Shaughnessy C, et al. Frequency and clinical consequences associated with sidebranch occlusion during stent implantation using zotarolimus-eluting and paclitaxel-eluting coronary stents. *Circ Cardiovasc Interv* 2009;2(02):133–139
- Nakazawa G, Yazdani SK, Finn AV, Vorpahl M, Kolodgie FD, Virmani R. Pathological findings at bifurcation lesions: the impact of flow distribution on atherosclerosis and arterial healing after stent implantation. *J Am Coll Cardiol* 2010;55(16):1679–1687
- Vassilev D, Gil RJ. Relative dependence of diameters of branches in coronary bifurcations after stent implantation in main vessel—importance of carina position. *Kardiol Pol* 2008;66(04):371–378, discussion 379
- Koo BK, Waseda K, Kang HJ, et al. Anatomic and functional evaluation of bifurcation lesions undergoing percutaneous coronary intervention. *Circ Cardiovasc Interv* 2010;3(02):113–119
- Medina A, Martín P, Suárez de Lezo J, et al. Vulnerable carina anatomy and ostial lesions in the left anterior descending coronary artery after floating-stent treatment. *Rev Esp Cardiol* 2009;62(11):1240–1249
- Nakamura S, Hall P, Maiello L, Colombo A. Techniques for Palmaz-Schatz stent deployment in lesions with a large side branch. *Cathet Cardiovasc Diagn* 1995;34(04):353–361
- Aliabadi D, Tilli FV, Bowers TR, et al. Incidence and angiographic predictors of side branch occlusion following high-pressure intracoronary stenting. *Am J Cardiol* 1997;80(08):994–997
- Fischman DL, Savage MP, Leon MB, et al. Fate of lesion-related side branches after coronary artery stenting. *J Am Coll Cardiol* 1993;22(06):1641–1646
- Ghayemian A, Nozari Y, Safir M, Mohammadpour RA. Predictors of side branch occlusion and its early complication after angioplasty in bifurcation lesions. *Pak J Med Sci* 2008;24(03):430–435