Original Article

Major Adverse Cardiovascular Events in Stenting Bifurcated Coronary Lesions: A Comparative Cross-Sectional Study of Provisional and Double-Stenting Methods

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ABSTRACT

Background: A coronary bifurcation lesion is defined as a stenosis located at the origin of a significant side branch. While the provisional approach is recognized as the gold standard, the two-stent strategy is proposed as a viable alternative. This study aimed to compare the incidence of major adverse cardiac events (MACE) between the provisional and double-stenting techniques.

Methods: A total of 280 patients with stenosis at the bifurcation of the coronary arteries were enrolled in the study. The variables examined included the location of the lesion in the coronary arteries, the extent of the coronary artery lesion, the treatment strategy (either double stenting or provisional stenting), and the incidence of MACE. Patients were followed up at 6 months and 1 year after angioplasty. Data were analyzed using SPSS software to compare the frequency of MACE between the 2 groups. A significance level of $P < 0.05$ was considered.

Results: Of the 280 participants, 219 were assigned to the provisional group, while the remaining participants were in the double-stenting group. A comparison of the 2 groups regarding vessel involvement and lesion site classification revealed that the highest frequency (75%) was associated with the left anterior descending artery and the diagonal branches. The most common complication observed during the first follow-up was recurrent angioplasty, occurring in 10.71% of participants. Additionally, 33.33% of the total participants in both groups underwent target vessel revascularization 1 year after angioplasty.

Conclusions: There was no significant difference in the occurrence of MACE between the provisional and double-stenting methods for treating coronary bifurcation lesions. ***(Iranian Heart Journal 2025; 26(2): 15-22)***

KEYWORDS: Major adverse cardiovascular events, Bifurcated coronary lesions, Provisional stenting method, Double-stenting method

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A coronary bifurcation lesion is defined as a stenosis located at the origin of a significant side branch. [1,2] Significant side branches are epicardial coronary artery branches ranging from medium to large that supply critical myocardial segments and can cause a risk of occlusion or impaired blood flow during percutaneous coronary intervention (PCI) of target lesions. [1,2] In addition, coronary artery bifurcations are responsible for 15%–20% of all PCI procedures. [3-5] Coronary artery bifurcations are still regarded as one of the most challenging lesions in interventional cardiology. [6] Plaque shift into the side branch can potentially compromise its flow, leading to higher rates of restenosis, stent thrombosis, and periprocedural myocardial infarction (MI). [7-9] The provisional approach, which uses a single stent for the main branch with ballooning of the side branch, is the gold standard approach for most bifurcation lesions. Nonetheless, double-stent implantation methods have been suggested as a treatment for patients with complex bifurcated lesions and relatively or significantly diseased side branches. [10] Despite current guidelines recommending the provisional single-stent procedure as the preferred approach (class I, level of evidence A), [2] the double-stent strategy is still considered a reasonable alternative in one-third of patients with complex true bifurcations. [11-13]

Some randomized clinical trials have investigated the role of provisional versus upfront double-stent bifurcation stenting techniques in coronary bifurcation lesions. Most of these studies have shown higher rates of major adverse cardiac events (MACE) with double-stent techniques, driven by higher periprocedural and late MI and stent thrombosis. [14]

The primary objective of this study was to compare MACE following provisional versus double stenting in coronary bifurcation lesions.

METHODS

This comparative cross-sectional study enrolled patients who underwent elective coronary bifurcation angioplasty, primary PCI, rescue PCI, or early invasive strategy between 2015 and 2018. All patients had coronary angiography and stenosis at the bifurcation of the coronary arteries. A bifurcation lesion was defined as a lesion at or near the main epicardial coronary artery division, including the main and side branches, with the larger side branch measuring at least 2.5 mm in diameter. Patients older than 75 years or with incurable malignancy and low survival prognosis (based on the opinion of an oncologist) were excluded from the study. The study variables were age, sex, cardiac risk factors (hypertension, diabetes mellitus, and hyperlipidemia), smoking status, coronary artery lesion location (the circumflex, obtuse marginal, right coronary, and left anterior descending arteries), coronary artery lesion extent, treatment strategy (double stenting or provisional stenting), and incidence of MACE, including acute MI, stroke, cardiac death, target vessel/lesion revascularization, hospitalization due to acute coronary syndrome (ACS), and decompensated heart failure.

Prior to angioplasty, antiplatelet drugs (aspirin 81–325 mg, clopidogrel 75–600 mg) were prescribed to all patients based on their drug use history. Angioplasty was performed as ad-hoc or staged PCI based on the patient's condition. The procedure was performed via the femoral approach, with local anesthesia (lidocaine) and insertion of an arterial sheath. The radial approach was used when patients could not remain in bed for an extended period or had peripheral arterial disease. Moreover, 0.014 guide

wires and 6 Fr and 7 Fr guiding catheters were used for angioplasty. Medicated stents, including the zotarolimus-eluting Resolute Onyx, XIENCE, Ultimaster, and Promus, were employed for stenting. For coronary bifurcation lesions with a side branch ≥ 2.5 mm, the provisional technique (single stent) was employed. If there was side branch compromise with thrombolysis in myocardial infarction (TIMI) flow grades 0 and I, chest pain, or ECG changes, side branch predilation was performed using a 1.5 mm balloon. If a TIMI flow grade of ≥ 1 could not be established, the balloon size was increased to ≥ 2 mm, and Kissing balloon inflation was performed. If a TIMI flow grade ≥ 1 could not be established or dissection occurred, double-stenting techniques using the small protrusion technique or the reverse crush method were employed. In the small protrusion technique, the following steps were performed sequentially: main branch stenting, proximal optimization technique, rewiring of the side branch, side branch predilation, side branch stenting, and final kissing balloon inflation.

During provisional technique angioplasty, both main and side branches were wired, followed by predilation of the main branch (based on anatomy) in some patients. Stent implantation was performed, followed by postdilation in all patients. In patients with TIMI flow grades 0 and I, side branch rewiring and ballooning with a 1.5 mm balloon was performed. If a TIMI flow grade ≥ 1 was not achieved, a ≥ 2 mm balloon was used, followed by final kissing balloon inflation. PCI was deemed successful if a TIMI flow grade 3 was achieved in the main branch and a TIMI flow grade ≥ 1 in the side branch, with no clinical symptoms or ECG changes. During PCI, 100 U/kg of unfractionated heparin was administered intravenously to all patients. In high-risk ACS patients, intracoronary loading dose or intravenous maintenance of glycoprotein IIb/IIIa inhibitor (eptifibatide) was prescribed if there was elevated troponin, inadequate pre-treatment with antiplatelet drugs, or a high volume of drug thrombus.

Patients were followed up at 6 months and 1 year after angioplasty. They were monitored for any readmission to a treatment center, repeat angiography (indicated for refractory chest pain, ACS, or second vessel angioplasty), cardiac or noncardiac death, and clinical status.

Statistical Analysis

Following data collection, the data were entered into SPSS software, version 21. To compare the frequency of MACE among the studied groups, we calculated the frequency, frequency percentage, and 95% confidence interval (CI). The χ^2 test was employed for analysis, and the Fisher exact test was used when the assumptions of the χ^2 test were not met. A significance level of $P < 0.05$ was established for all tests in this study. To control for confounding variables, we conducted a multiple regression analysis at the conclusion of the study.

Ethical Approval

All participants provided informed consent before their inclusion in the study. The study protocol received approval from the Scientific Vice Chancellor for Research and the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1399.546). The study adhered to the ethical guidelines outlined in the 1975 Declaration of Helsinki.

RESULTS

This study analyzed data from 280 patients to compare MACE associated with provisional versus double-stenting methods for coronary artery bifurcation lesions. Of the total patients, 219 (155 men and 64 women) were in the provisional group with a mean age of

58.60 ± 9.72 years, and 61 patients (38 men and 23 women) with a mean age of 56.85 ± 10.08 years were in the double-stenting group. The youngest person studied was 33 years old, while the oldest one was 75.

The comparison of EF between the 2 studied groups showed a mean value of 43.84 ± 10.34 in the provisional group and 45.66 ± 9.46 in the double-stenting group, with no statistically significant difference ($P = 0.196$).

Table 1 depicts the comparison of diabetes mellitus, hypertension, hyperlipidemia, and smoking between the provisional and double-stenting groups.

Table 1. Comparisons of diabetes mellitus, hypertension, hyperlipidemia, and smoking between the 2 study groups

Risk Factors	Provisional	Double-Stenting	*P**
	n (%)	n (%)	
Diabetes mellitus	60 (27.4)	13 (21.3)	0.34
Hypertension	110 (50.2)	34 (55.7)	0.45
Hyperlipidemia	85 (38.8)	13 (21.3)	0.01
Smoking	77 (35.2)	21 (34.4)	0.91

Table 2 presents the comparison of the types of hospitalization between the provisional and double-stenting groups.

Table 2. Comparisons of types of hospitalization between the 2 study groups

Types of Hospitalization			Provisional	Double-Stenting	Total	*P*
			N (%)	N (%)	N (%)	
Elective			55 (25.1)	45 (73.8)	100 (35.7)	<0.001
Urgent	STEMI	Primary PCI	38 (17.4)	4 (6.6)	42 (15)	
		Rescue PCI	16 (7.2)	3 (4.8)	19 (6.7)	
	NSTEACS	NSTEMI	17 (7.8)	0	17 (6.1)	
		Neglected MI	15 (6.9)	2 (3.3)	17 (6.1)	
		UA	78 (35.6)	7 (11.5)	85 (30.4)	
Total			219 (100)	61 (100)	280 (100)	

PCI: percutaneous coronary intervention, NSTEMI: non–ST-elevation myocardial infarction, UA: unstable angina, NSTACS: non–ST-acute coronary syndrome

A comparison of angioplasty techniques between the provisional and double-stenting groups is presented in Table 3.

Table 3. Comparisons of angioplasty techniques between the 2 study groups

Type of Technique	Provisional	Double-Stenting	*P*
	n (%)	n (%)	
Side branch ballooning	7 (3.2)	61 (100)	0.001
Final kissing balloon inflation	18 (8.2)	61 (100)	<0.001
Eptifibatide injection	13 (5.9)	3 (4.9)	0.999

The comparison of the 2 groups concerning vessel involvement and lesion site classification revealed the highest frequency (75%) in the left anterior descending artery (between the main vessels) and the diagonal artery (between the side vessels). The distribution of the frequency of main and collateral vessel involvement was significantly different between the groups ($P < 0.001$).

As Table 4 shows, the most frequent complication in the first follow-up (6 months after angioplasty) was recurrent angioplasty, occurring in 10.71% of participants.

Table 5 demonstrated that 33.33% of participants in both groups underwent target vessel revascularization 1 year after angioplasty.

Table 4. Comparisons of MACE between the 2 study groups 6 months after angioplasty

MACE		Provisional N (%)	Double-Stenting N (%)	Total N (%)	*P*
Primary Outcomes	Cardiac death	0	2 (3.28)	2 (0.71)	0.04
Secondary Outcomes	MI	0	1 (1.64)	1 (0.36)	0.22
	Stroke	1 (0.46)	0	1 (0.36)	0.78
	Hospitalization with ACS	10 (4.57)	2 (3.28)	12 (4.29)	0.49
	Hospitalization with DHF	0	0	0	-
	Noncardiac death	2 (0.91)	1 (1.69)	3 (1.08)	0.51
	CABG	1 (4.17)	0	1 (3.33)	0.8
	Recurrent angiography	24 (10.96)	6 (9.84)	30 (10.71)	0.51
	TVR	0	0	0	-
	TLR	0	0	0	-

MACE: major adverse cardiovascular events, MI: myocardial infarction, ACS: acute coronary syndrome, DHF: decompensated heart failure, CABG: coronary artery bypass grafting, TVR: target vessel revascularization, TLR: target lesion revascularization

Table 5. Comparisons of MACE between the 2 study groups 1 year after angioplasty

MACE		Provisional N (%)	Double-Stenting N (%)	Total N (%)	*P*
Primary Outcomes	Cardiac death	5 (2.30)	1 (1.72)	6 (2.18)	0.63
Secondary Outcomes	MI	0	1 (1.7)	1 (0.04)	0.21
	Stroke	0	0	0	-
	Hospitalization with ACS	0	5 (8.86)	5 (1.82)	0.001
	Hospitalization with DHF	2 (0.92)	0	2 (0.73)	0.62
	Noncardiac death	2 (0.94)	0	2 (0.74)	0.62
	CABG	0	3 (50)	3 (25)	0.1
	Recurrent angiography	6 (2.76)	6 (10.34)	12 (4.36)	0.02
	TVR	1 (16.67)	3 (50)	4 (33.33)	0.28
	TLR	0	0	0	-

MACE: major adverse cardiovascular events, MI: myocardial infarction, ACS: acute coronary syndrome, DHF: decompensated heart failure, CABG: coronary artery bypass grafting, TVR: target vessel revascularization, TLR: target lesion revascularization

DISCUSSION

This study compared MACE in 280 patients at 2 follow-up intervals (6 months and 1 year) after coronary artery bifurcation stenting using the provisional and double-stenting methods. The provisional group consisted of 219 patients with a mean age of 58.60 ± 9.72 years, while the double-stenting group was composed of 61 patients with a mean age of 56.85 ± 10.08 years. No statistically significant difference was observed in recurrent MI between the provisional and double-stenting groups at both follow-up intervals (6 months and 1 year) after angioplasty. A 10-year follow-up study by D'Ascenzo et al [15] investigating long-term outcomes of unprotected left main bifurcation disease reported no significant difference in recurrent MI between the provisional and double-stenting techniques after angioplasty, chiming with our results. These findings were corroborated by Leus et al. [13] In contrast, Nairooz et al [4] reported a lower frequency of MI in the provisional group than in the double-stenting group. The comparison of cardiac death, hospitalization with heart failure, coronary artery bypass grafting, recurrent angiography, and target vessel revascularization following coronary bifurcation stenting in this study showed no significant difference between the

provisional and double-stenting groups, consistent with the findings of Kumsar et al. [16] Zhang et al [17] reported a procedural success rate of 98.8% for the provisional technique and 98.5% for the double-stenting technique in a multicenter, randomized trial. Likewise, no significant difference in MACE frequency after PCI using different stenting techniques was observed in other studies. [18,19] However, Yurtdas et al [20] reported that double-stenting was a safe and feasible technique for coronary bifurcation lesions in patients with ACS, with a relatively low MACE incidence during the follow-up period. While more research is needed to draw definitive conclusions, our results suggest that the provisional and double-stenting techniques do not significantly differ concerning MACE during the follow-up periods examined. Mathew et al [21] reported that diabetes might be associated with 9-month mortality and increased target vessel revascularization rates in patients undergoing PCI. Consistent with their findings, our study found a higher incidence of MACE after PCI in diabetic patients than in non-diabetic patients (15% vs 5%; $P = 0.025$).

Diabetes is linked to a poorer prognosis in patients compared to their non-diabetic counterparts. Diabetic patients face an increased risk of restenosis after PCI, as well as a higher likelihood of target lesion revascularization and decreased left ventricular function at a 6-month follow-up. [22,23] Therefore, the impact of diabetes on PCI outcomes cannot be overlooked. Studies have been conducted to investigate the effect of diabetes on PCI outcomes, [21] to compare different types of bare-metal stents and drug-eluting stents, [22] and to evaluate mortality rates associated with PCI in diabetic patients. [23] Despite extensive research on PCI outcomes in diabetic patients, no study was found that directly compares the different stenting techniques used in this population. Still, our results suggest that diabetic patients may require closer monitoring and follow-up, as they are at higher risk for adverse events after PCI.

In terms of hospitalization due to ACS in our study's follow-up, 5 (1.8%) of our patients suffered acute cardiac attacks, all of whom were from the double-stenting group (8.6%). This difference was statistically significant ($P = 0.001$). While previous studies did not address hospitalization due to acute coronary syndrome separately, our findings indicate that patients who underwent double-stenting were more likely to be hospitalized with an acute coronary syndrome during the 6-month to 1-year follow-up period. Nevertheless, more studies are needed to confirm this finding with certainty.

CONCLUSIONS

To summarize, both provisional and double-stent techniques were found to be equally effective in terms of MACE occurrence, with no statistically significant difference between the two methods in treating coronary bifurcation lesions. Therefore, clinicians can select either technique based on their clinical judgment.

Declarations

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Conflict of Interest

The authors declare that they have no competing interests.

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