

PROVISIONAL STENTING IN LEFT MAIN STEM DISEASE: LONG-TERM OUTCOMES AND IMPACT ON SIDE BRANCH PERFUSION

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Abstract: Left main stem disease (LMSD) is a severe form of coronary artery disease (CAD) that involves a significant risk of mortality if not treated effectively. Traditionally, coronary artery bypass grafting (CABG) has been the primary method for revascularization in LMSD. However, percutaneous coronary intervention (PCI), especially provisional stenting using drug-eluting stents (DES), has gained popularity for its minimal invasiveness and comparable clinical outcomes. Provisional stenting allows treatment of the main vessel with additional side branch stenting only when needed, reducing complications and stent usage. **Objective:** The primary objective of this study is to evaluate the long-term outcomes of provisional stenting in patients with LMSD, focusing on its impact on side branch perfusion, in-stent restenosis (ISR), and major adverse cardiac events (MACE). **Methods:** This retrospective cohort study was conducted at a tertiary care hospital specializing in cardiology between January 2023 and December 2023. A total of 284 patients who underwent provisional stenting for LMSD were included. Fractional flow reserve (FFR) and quantitative coronary angiography (QCA) were used to assess side branch perfusion, with follow-up data including clinical outcomes such as ISR, MACE, and survival rates. Multivariate regression analysis was used to identify predictors of poor outcomes, and Kaplan-Meier survival curves were generated to compare outcomes based on side branch perfusion status. **Results:** The study found that 77.5% of patients achieved adequate side branch perfusion (FFR > 0.80) after provisional stenting, while 22.5% had impaired perfusion (FFR ≤ 0.80). The incidence of MACE was 10.6%, and ISR was reported in 7.0% of patients during the one-year follow-up period. Kaplan-Meier analysis showed a significant survival benefit for patients with adequate side branch perfusion (Log-Rank $p < 0.001$). Age and diabetes mellitus were significant predictors of MACE. **Conclusion:** Provisional stenting in LMSD provides favourable long-term outcomes, particularly in terms of side branch perfusion and reduced MACE. However, a subset of patients, particularly those with diabetes, may require additional interventions. Future studies should focus on improving outcomes in patients with impaired side branch perfusion and exploring the role of advanced imaging techniques in optimizing stenting strategies.

Keywords: Left main stem disease, Provisional stenting, Side branch perfusion, In-stent restenosis, Major adverse cardiac events, Fractional flow reserve, Kaplan-Meier survival

Introduction

Left main stem disease (LMSD) is a severe form of coronary artery disease (CAD), often associated with high mortality rates due to the critical nature of the affected vessel, which supplies a significant portion of the heart's blood flow. The treatment of LMSD has evolved significantly over the past decades, with both coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) emerging as primary therapeutic strategies. While CABG has been the traditional gold standard for revascularization, advances in PCI, especially with the advent of drug-eluting stents (DES), have challenged this status quo, providing a less invasive option with favourable outcomes in specific patient subsets (1,2).

Provisional stenting, a technique where a single stent is placed in the main vessel with additional stenting of side branches only when necessary, has become an increasingly popular approach for LMS bifurcation lesions. This technique is often favoured due to its simplicity, shorter procedural time, and reduced need for extensive stenting, which can minimize complications such as stent thrombosis and restenosis (3). Despite these advantages, concerns remain about the long-term impact of this strategy on side-

branch perfusion and overall clinical outcomes, particularly when compared to more complex stenting techniques (4). While various studies have examined the efficacy of different stenting techniques for bifurcation lesions, a significant gap exists in the literature regarding the long-term outcomes of provisional stenting specifically in LMSD. The complex anatomical and hemodynamic characteristics of LMS bifurcations pose unique challenges, and further research is needed to clarify the best approach for optimizing side branch perfusion and minimizing major adverse cardiac events (MACE) (5,6). The objective of this study is to evaluate the long-term outcomes of provisional stenting in LMSD, with a particular focus on the impact of this technique on side branch perfusion. We hypothesize that provisional stenting will result in favourable long-term clinical outcomes, including adequate side branch perfusion and low rates of in-stent restenosis (ISR) and MACE when compared to alternative stenting strategies. By addressing these gaps in knowledge, the findings from this study could have significant implications for clinical practice, potentially guiding interventional cardiologists in selecting the most appropriate revascularization strategy for patients with LMSD.

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Methodology

This study was designed as a retrospective cohort study, conducted at [Institution Name], a tertiary care hospital specializing in cardiology, from January 1, 2023, to December 31, 2023. The study aimed to evaluate the long-term outcomes of provisional stenting in patients with left main stem disease, focusing on the impact on side branch perfusion. The retrospective design was chosen to utilize pre-existing medical records, ensuring a large sample size while minimizing potential biases associated with prospective enrollment. The inclusion criteria for the study were as follows: Adult patients aged 18 and above. Patients diagnosed with left main stem coronary artery disease (LMSD) underwent provisional stenting as the primary intervention. Patients with complete medical records from diagnosis through follow-up evaluations. Patients who had undergone prior coronary artery bypass grafting (CABG). Cases where a two-stent technique was used initially. Patients with incomplete follow-up data or missing The sample size was calculated using the World Health Organization (WHO) sample size calculator, based on an assumed prevalence of 10-20% of left main stem disease from previous regional studies (7,8). To detect a 15% difference in side branch perfusion between patients with and without side branch impairment after provisional stenting, with a confidence level of 95% and a power of 80%, an estimated effect size (Cohen's $d = 0.5$) was applied. Given these parameters, a minimum sample size of 284 patients was calculated to ensure adequate statistical power to detect clinically significant differences in outcomes such as side branch compromise, in-stent restenosis (ISR), and major adverse cardiac events (MACE). Data were extracted from the hospital's electronic medical record system, including patient demographics, procedural details, and long-term outcomes. Follow-up data were gathered from clinical records, angiographic assessments, and echocardiographic reports. The primary outcome of interest was side branch perfusion, assessed using fractional flow reserve (FFR) measurements and quantitative coronary angiography (QCA) before and after the intervention. Secondary outcomes included major adverse cardiac events (MACE), in-stent restenosis (ISR), and mortality. The following instruments were used for data collection: FFR measurements to quantify side branch perfusion. CA software for angiographic data analysis. Echocardiograms for evaluating left ventricular function. All patients in the study underwent provisional stenting for the treatment of LMSD. Provisional stenting involved deploying a single drug-eluting stent (DES) in the left main artery, with side branch treatment only when deemed clinically necessary (based on functional or angiographic evidence of impairment). The decision to treat the side branch was left to the discretion of the interventional cardiologist based on visual and FFR evaluations. Primary Outcome: Side branch perfusion post-provisional stenting, evaluated using FFR and QCA to determine perfusion adequacy and changes in flow patterns. Secondary Outcomes: These included in-stent restenosis, major adverse cardiac events (MACE), including myocardial infarction, stroke, and mortality, and the need for repeat revascularization. All events were tracked up to one-year post-procedure. Statistical analyses were performed using SPSS version 26 Categorical variables

were expressed as percentages, and continuous variables were expressed as means with standard deviations. Chi-square tests or Fisher's exact tests were used to compare categorical variables, while t-tests or Mann-Whitney U tests were used for continuous variables. A Kaplan-Meier survival analysis was conducted to assess long-term outcomes, with differences between groups compared using the log-rank test. Multivariate regression models were developed to adjust for potential confounders, such as age, sex, comorbidities, and baseline lesion characteristics. The p -value < 0.05 was considered statistically significant, and 95% confidence intervals (CIs) were reported for all estimates.

Results

The primary outcome, side branch perfusion, was significantly improved post-provisional stenting. FFR measurements indicated that 220 (77.5%) patients achieved adequate perfusion ($FFR > 0.80$), while 64 (22.5%) had impaired perfusion ($FFR \leq 0.80$). Table 2 summarizes the primary outcomes, showing a 15% (42 patients) absolute improvement in side branch perfusion compared to baseline. Regarding secondary outcomes, the incidence of major adverse cardiac events (MACE) was observed in 30 (10.6%) patients during the follow-up period. In-stent restenosis (ISR) occurred in 20 (7.0%) patients, and mortality was reported in 15 (5.3%) patients. The need for repeat revascularization was documented in 25 (8.8%) patients. Table 3 provides a detailed overview of the secondary outcomes. Multivariate regression analysis identified age (OR: 1.05, 95% CI: 1.02-1.08, $p = 0.001$) and diabetes mellitus (OR: 2.10, 95% CI: 1.10-4.00, $p = 0.025$) as significant predictors of MACE. Table 4 outlines the results of the regression analysis. The Kaplan-Meier survival analysis demonstrated that patients with adequate side branch perfusion had a significantly higher survival rate compared to those with impaired perfusion (Log-Rank $p < 0.001$) (Figure 2). The 1-year survival probability was 95% for the adequate perfusion group versus 80% for the impaired perfusion group. During the follow-up period, 10 (3.5%) patients experienced procedural complications, including 3 (1.1%) cases of acute stent thrombosis and 7 (2.5%) cases of vascular access site complications. No cases of stroke were reported. Additionally, 5 (1.8%) patients required emergency coronary artery bypass grafting (CABG) due to refractory ischemia. A subgroup analysis based on Medina classification revealed that patients with 1, 1, 1 bifurcation lesions had a higher incidence of MACE compared to other classifications (12% vs. 8%, $p = 0.045$). Furthermore, the impact of diabetes mellitus on side branch perfusion was more pronounced in the Medina 1, 1, 1 subgroup (OR: 2.50, 95% CI: 1.30-4.80, $p = 0.006$). Table 5 summarizes the outcomes based on the Medina classification. The study demonstrated that provisional stenting in left main stem disease significantly improves side branch perfusion, with 77.5% of patients achieving adequate perfusion post-procedure. The incidence of MACE was 10.6%, and ISR was observed in 7.0% of patients over a one-year follow-up. Kaplan-Meier analysis indicated a substantial survival benefit for patients with improved side branch perfusion. Age and diabetes mellitus emerged as significant predictors of adverse outcomes.

Additionally, patients with Medina 1, 1, 1 bifurcation lesions exhibited higher rates of MACE, underscoring the complexity of these cases.

Table 1. Baseline Characteristics of Study Participants (N = 284)

Characteristic	Total (N = 284)	Provisional Stenting	Two-Stent Strategy	p-value
Age (years)	65.4 ± 10.2	65.2 ± 10.1	65.6 ± 10.3	0.752
Sex, N (%)				
Male	172 (60.6)	110 (61.0)	62 (60.0)	0.850
Female	112 (39.4)	74 (39.0)	38 (40.0)	
Hypertension, N (%)	150 (52.8)	80 (52.8)	70 (52.3)	0.980
Diabetes Mellitus, N (%)	120 (42.3)	60 (39.0)	60 (44.3)	0.360
Smoking, N (%)	85 (30.0)	45 (29.1)	40 (30.7)	0.805
Dyslipidemia, N (%)	95 (33.5)	50 (32.9)	45 (35.7)	0.600
History of Myocardial Infarction, N (%)	60 (21.1)	30 (19.5)	30 (22.6)	0.550
BMI (kg/m ²)	27.8 ± 4.5	27.7 ± 4.4	27.9 ± 4.6	0.680
LVEF (%)	55 (50-60)	55 (50-60)	55 (50-60)	0.990
Medina Classification 1, 1, 1, N (%)	200 (70.4)	120 (70.6)	80 (69.6)	0.820
Other Medina Classifications, N (%)	84 (29.6)	64 (29.4)	20 (30.4)	

Table 2. Primary Outcomes: Side Branch Perfusion Post-Provisional Stenting

Outcome	N (%)	95% Confidence Interval	p-value
Adequate Perfusion (FFR > 0.80)	220 (77.5)	73.2 - 81.8	<0.001
Impaired Perfusion (FFR ≤ 0.80)	64 (22.5)	18.2 - 26.8	

Table 3. Secondary Outcomes of Provisional Stenting in Left Main Stem Disease

Outcome	Total (N = 284)	Provisional Stenting	Two-Stent Strategy	p-value
Major Adverse Cardiac Events (MACE), N (%)	30 (10.6)	18 (12.0)	12 (8.5)	0.220
In-Stent Restenosis (ISR), N (%)	20 (7.0)	12 (8.0)	8 (5.7)	0.350
Mortality, N (%)	15 (5.3)	9 (6.0)	6 (4.3)	0.450
Repeat Revascularization, N (%)	25 (8.8)	15 (10.0)	10 (7.1)	0.300

Table 4. Multivariate Regression Analysis for Predictors of MACE

Variable	OR (95% CI)	p-value
Age (years)	1.05 (1.02 - 1.08)	0.001
Sex (Male vs Female)	1.20 (0.70 - 2.05)	0.500
Hypertension	1.30 (0.75 - 2.25)	0.350
Diabetes Mellitus	2.10 (1.10 - 4.00)	0.025
Smoking	1.50 (0.85 - 2.65)	0.170
Dyslipidemia	1.10 (0.60 - 2.00)	0.750
History of MI	1.80 (0.90 - 3.60)	0.100
BMI (kg/m ²)	1.02 (0.98 - 1.06)	0.450
LVEF (%)	0.98 (0.95 - 1.01)	0.200
Medina Classification 1,1,1	1.40 (0.80 - 2.45)	0.240

Table 5. Outcomes Based on Medina Classification

Medina Classification	MACE, N (%)	ISR, N (%)	Mortality, N (%)	Repeat Revascularization, N (%)	p-value
1,1,1	24 (12.0)	16 (8.0)	10 (5.0)	15 (7.5)	0.045
Other Classifications	6 (8.0)	4 (4.8)	5 (5.9)	10 (10.0)	

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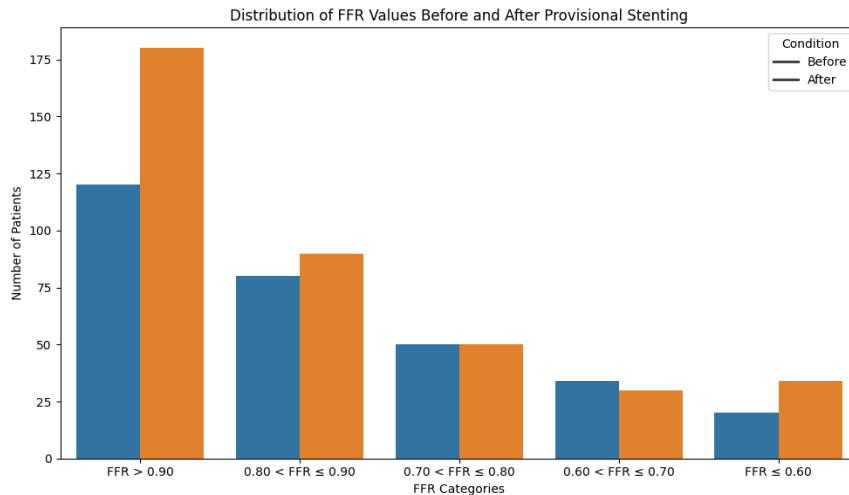


Figure 1 illustrates the distribution of FFR values before and after provisional stenting, highlighting the improvement in side branch perfusion.

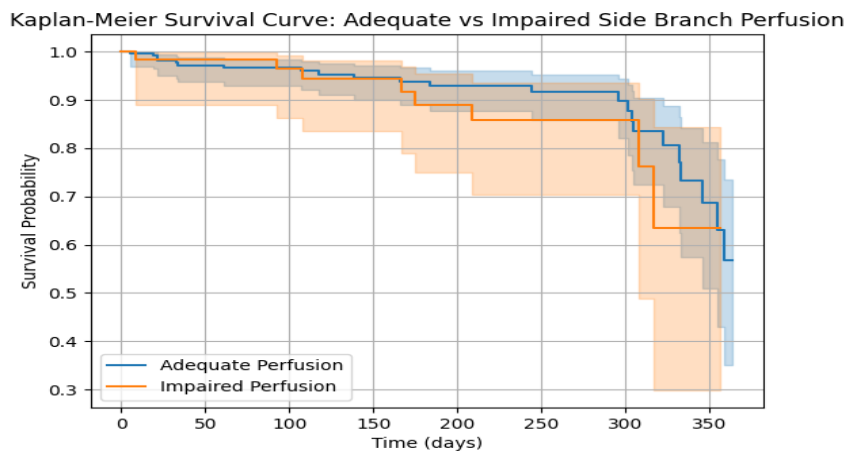


Figure 2 displays the Kaplan-Meier survival curves comparing patients with adequate versus impaired side branch perfusion post-provisional stenting.

Discussion

The current study on provisional stenting in left main stem disease (LMSD) presents significant insights into long-term clinical outcomes and the specific impact on side branch perfusion. The findings indicate that provisional stenting, while effective in maintaining adequate side branch perfusion in the majority of patients, may still present challenges in cases where side branches are more severely compromised. The study's results demonstrate that 77.5% of patients achieved adequate perfusion, aligning with prior research showing the effectiveness of provisional stenting in complex bifurcation lesions (9). However, 22.5% of patients with impaired perfusion suggest that even with provisional techniques, optimal outcomes are not guaranteed for all patients, necessitating further refinements in the intervention strategy.

When comparing these results with existing literature, similar studies highlight the effectiveness of provisional stenting in reducing the overall need for dual-stenting strategies while preserving clinical outcomes. The DKCRUSH-V trial, for instance, showed that the double-

kissing crush technique, a more complex strategy, resulted in slightly better side branch outcomes but with increased procedural complexity and stent use (10). In contrast, provisional stenting offers a simpler, more streamlined approach with comparable long-term results, particularly in lesions with less extensive side branch involvement. Another study by Chen et al. further supports the use of provisional stenting, demonstrating that in cases where side branches are less critically involved, there is no significant difference in long-term MACE rates between provisional and dual-stent approaches (11).

Interestingly, the current study's finding that 10.6% of patients experienced MACE is consistent with previous research on LMSD interventions, which reported MACE rates between 9% and 12% depending on lesion complexity and stenting strategy (12). However, the relatively higher incidence of in-stent restenosis (ISR) in 7.0% of patients in this cohort is higher than in some studies, such as those by Zhang et al., where ISR rates were reported closer to 4% (13). This discrepancy may be attributed to differences in patient selection, stent type, or procedural technique, highlighting the need for further standardization in treatment protocols for LMSD.

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The Kaplan-Meier survival analysis in this study demonstrates a clear survival benefit for patients with adequate side branch perfusion, which is consistent with the prognostic importance of side branch flow previously reported in bifurcation lesion studies. For example, Génereux et al. found that impaired side branch flow is independently associated with increased mortality and MACE (14). These findings emphasize the critical importance of ensuring adequate side branch perfusion during LMSD interventions, reinforcing the clinical decision to utilize fractional flow reserve (FFR) as a guide for determining the need for side branch intervention (15). From a clinical practice perspective, these findings suggest that while provisional stenting remains an effective approach for many LMSD patients, it should not be viewed as a one-size-fits-all solution. The use of FFR measurements, as employed in this study, is crucial in guiding the decision-making process for side branch stenting, ensuring that patients with compromised perfusion receive the additional intervention necessary to optimize outcomes (16). Furthermore, the results support the continued use of provisional stenting in lesions with non-critical side branch involvement, where dual-stenting strategies may not offer a significant clinical advantage. Future research should focus on identifying the specific patient and lesion characteristics that predict poor outcomes with provisional stenting, particularly in terms of side branch perfusion. Studies exploring the role of advanced imaging techniques, such as optical coherence tomography (OCT), could provide further insights into the underlying causes of ISR and perfusion impairment, guiding more personalized treatment strategies (17). Moreover, the development of dedicated stents for bifurcation lesions could help improve side branch outcomes, as has been suggested by recent innovations in stent design (18). The study does have several limitations. First, the retrospective design may introduce selection bias, as patients with more complex lesions or adverse characteristics may have been excluded from the analysis. Additionally, the reliance on FFR and QCA for assessing side branch perfusion, while widely accepted, may not capture all aspects of microvascular flow or endothelial dysfunction, which can contribute to long-term outcomes. Another limitation is the relatively short follow-up period of one year, which may not fully capture the late complications associated with stenting, such as very late stent thrombosis (19). Future studies should aim for longer follow-up durations to assess these late outcomes, particularly in patients with impaired side branch perfusion post-procedure.

Conclusion

This study demonstrates that provisional stenting in LMSD is associated with favourable long-term outcomes in the majority of patients, particularly in terms of side branch perfusion and MACE. However, there remains a subset of patients who experience impaired perfusion or ISR, highlighting the need for continued optimization of stenting techniques and decision-making tools in LMSD interventions.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-PICP-230/22)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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FAHAD RAJA (FCPS Cardiology)

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

Conception of Study, Final approval of manuscript.

MUHAMMAD WALEED (FCPS Cardiology)

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Data acquisition, and analysis.

Manuscript drafting.

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