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Original research article

PRIMARY PCI FOR MULTIVESSEL DISEASE: EXPLORING THE OPTIMAL STRATEGY FOR CORONARY REVASCULARIZATION

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Abstract: *Multivessel coronary artery disease (CAD) presents a significant challenge in patients with acute coronary syndromes (ACS). Primary percutaneous coronary intervention (PCI) is a widely accepted treatment strategy for high-risk patients, including those with ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI). However, whether immediate multivessel PCI or staged PCI leads to better outcomes remains an area of ongoing research.* ***Objective:*** *This study aims to compare the clinical outcomes between immediate multivessel PCI and staged PCI in patients with multivessel CAD undergoing primary PCI.* ***Methods:*** *This retrospective cohort study was conducted at a tertiary care center, collecting data from 1st March 2023, to 31st March 2024. The study included 200 patients aged 18 years and older diagnosed with ACS and multivessel disease, defined as stenosis ≥70% in at least two coronary arteries. Patients were categorized into two groups based on the PCI strategy (immediate multivessel PCI vs. staged PCI). The primary endpoint was major adverse cardiovascular events (MACE), a composite of all-cause mortality, myocardial infarction, target vessel revascularization, and stent thrombosis. Secondary outcomes included recurrent angina, heart failure requiring hospitalization, and bleeding complications. Statistical analysis was performed using SPSS version 26.0, and survival analysis was conducted using the Kaplan-Meier method.* ***Results:*** *MACE occurred in 48 patients (24%) during the one-year follow-up. The staged PCI group showed significantly lower MACE rates (16%) compared to the immediate PCI group (32%, $p = 0.005$). Recurrent angina was also less frequent in the staged PCI group (10%) compared to the immediate PCI group (18%, $p = 0.046$). Multivariate analysis identified diabetes mellitus (HR: 2.4, $p < 0.001$) and CKD (HR: 2.1, $p = 0.002$) as independent predictors of MACE.* ***Conclusion:*** *Staged PCI offers superior outcomes compared to immediate multivessel PCI in patients with multivessel CAD, particularly those with diabetes and CKD. These findings suggest that individualized revascularization strategies may improve long-term cardiovascular outcomes in high-risk populations.*

Keywords: Primary PCI, multivessel disease, acute coronary syndrome, staged PCI, major adverse cardiovascular events, diabetes, chronic kidney disease.

Introduction

Multivessel coronary artery disease (CAD) presents a significant challenge in the management of patients with acute coronary syndromes (ACS), especially those who require revascularization. Among these, primary percutaneous coronary intervention (PCI) is a widely accepted strategy for treating patients with acute ST-elevation myocardial infarction (STEMI) or high-risk non-ST-elevation myocardial infarction (NSTEMI) (1). However, patients with multivessel disease undergoing primary PCI face unique difficulties, as they are at a higher risk of recurrent ischemia and adverse cardiovascular events due to the involvement of multiple coronary arteries. Immediate multivessel PCI versus a staged PCI approach remains a subject of ongoing debate (2).

Current guidelines recommend treating the infarct-related artery (IRA) first during the index procedure, followed by potential staged revascularization of the non-culprit arteries, but there is variability in practice and outcomes across different centers (3). Immediate multivessel PCI may reduce the need for further procedures but carries a potential risk of peri-procedural complications, including stent thrombosis and bleeding, while staged PCI allows for recovery between interventions, potentially minimizing risk (4). Therefore, there is a critical need to determine the most optimal PCI strategy for patients with multivessel disease to improve outcomes and reduce complications (5).

This study aims to address this gap by comparing the clinical outcomes of immediate versus staged PCI in patients with multivessel disease. The primary hypothesis is that staged PCI will result in lower rates of major adverse cardiovascular events (MACE) compared to immediate multivessel PCI due to better patient stabilization between interventions. Additionally, the study seeks to identify which patient subgroups, such as those with diabetes mellitus or chronic kidney disease, may benefit more from one approach over the other.

The results of this study have the potential to significantly impact clinical practice by providing evidence for tailored revascularization strategies in multivessel disease. By identifying the most effective approach to PCI, clinicians will be better equipped to reduce procedural risks, optimize long-term outcomes, and enhance the quality of care for high-risk patients (6).

Methodology

This study was designed as a retrospective cohort study to evaluate the optimal strategy for coronary revascularization in patients with multivessel coronary artery disease (CAD) who underwent primary percutaneous coronary intervention

(PCI). The study was conducted at Lady Reading Hospital Peshawar Pakistan, a tertiary care center with specialized interventional cardiology services. The data collection period spanned from 1st March 2023, to 31st March 2024, , to ensure a comprehensive assessment of clinical outcomes during a one-year follow-up period. Etical approval for the study was obtained from the Institutional Review Board (IRB), and patient data confidentiality was strictly maintained according to the principles of the Declaration of Helsinki.

The study included patients aged 18 years and older who were admitted with acute coronary syndrome (ACS) and diagnosed with multivessel disease. Multivessel disease was defined as the presence of stenosis ≥70% in at least two major coronary arteries, including the left anterior descending artery (LAD), left circumflex artery (LCx), and right coronary artery (RCA). To be eligible, participants had to meet the following inclusion criteria:

- Diagnosed with ST-elevation myocardial infarction (STEMI) or high-risk non-ST-elevation myocardial infarction (NSTEMI).
- Underwent primary PCI with at least one stent placement.
- Complete follow-up data available for 12 months post-procedure.

Exclusion criteria were:

- Patients with previous coronary artery bypass grafting (CABG) or PCI in the last 6 months.
- Patients with incomplete medical records or missing follow-up data.
- Patients with contraindications for PCI or stent implantation, such as severe left main coronary artery disease requiring CABG.

All patients underwent primary PCI as the initial revascularization strategy. The procedure involved stent placement in the infarct-related artery (IRA), followed by staged PCI or immediate multivessel PCI based on the interventional cardiologist's discretion. Staged PCI was typically performed within 2-6 weeks after the index procedure. Drug-eluting stents (DES) were preferred, although bare-metal stents (BMS) were used in select cases where DES was contraindicated. Standard pre- and post-PCI medications were administered, including dual antiplatelet therapy (aspirin and a P2Y12 inhibitor), statins, beta-blockers, and ACE inhibitors.

The primary outcome of this study was the incidence of major adverse cardiovascular events (MACE) at 12 months. MACE was defined as a composite of:

- All-cause mortality.
- Myocardial infarction (MI).
- Target vessel revascularization (TVR).
- Stent thrombosis.

The secondary outcomes included:

- Recurrent angina.
- Incidence of heart failure requiring hospitalization.
- Bleeding complications, classified according to the Bleeding Academic Research Consortium (BARC) criteria.

Patient data were collected retrospectively from the hospital's electronic medical records (EMR) system. The data collection process was standardized to minimize variability and bias. Information was gathered on patient demographics, clinical presentation, angiographic findings, procedural details, and follow-up outcomes. Follow-up data were obtained from outpatient clinic visits, telephone interviews, and review of hospital readmissions. Data on medication adherence, lifestyle modifications, and any adverse events during the follow-up period were also documented.

The sample size was calculated based on the estimated prevalence of adverse cardiovascular events in patients with multivessel disease undergoing primary PCI. Previous studies have shown that the event rate for MACE in similar populations ranges from 20% to 30% (8,9). Using this prevalence estimate, we calculated a sample size of 200 patients to detect a significant difference in MACE rates with 80% power and a 5% significance level ($\alpha = 0.05$), accounting for a 10% attrition rate due to loss to follow-up or incomplete data. The sample size calculation was performed using the World Health Organization (WHO) sample size calculator designed for cohort studies.

Data were analyzed using SPSS version 26.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]), depending on the distribution of the data. Categorical variables were expressed as frequencies and percentages. The comparison between groups (immediate multivessel PCI vs. staged PCI) was performed using the Student's t-test or Mann-Whitney U test for continuous variables, and the Chi-square test or Fisher's exact test for categorical variables.

Survival analysis was conducted using the Kaplan-Meier method to estimate the time to MACE, with differences between groups assessed using the log-rank test. To identify independent predictors of MACE, a Cox proportional hazards regression model was used, adjusting for potential confounders such as age, gender, diabetes mellitus, hypertension, and type of stent used. Hazard ratios (HR) with 95% confidence intervals (CI) were reported. A p-value of less than 0.05 was considered statistically significant.

The study was conducted in compliance with ethical standards outlined by the Declaration of Helsinki. Given the retrospective nature of the study, informed consent was waived; however, confidentiality was maintained by de-identifying all patient data. Ethical approval was obtained from the Institutional Review Board (IRB) of Lady Reading Hospital Peshawar.

Results

This study analyzed the outcomes of 200 patients with multivessel coronary artery disease (CAD) who underwent primary percutaneous coronary intervention (PCI) between January 1, 2023, and December 31, 2023. The primary objective was to compare clinical outcomes between patients who received immediate multivessel PCI versus those who underwent staged PCI. A detailed analysis of the patient characteristics, procedural details, and both primary and secondary outcomes is presented below.

Of the 200 patients, 130 (65%) were male and 70 (35%) were female. The mean age of the cohort was 64.3 years (SD ± 9.5), with a median age of 65 years. The incidence of comorbidities included hypertension in 146 patients (73%), diabetes mellitus in 108 patients (54%), and chronic kidney disease (CKD) in 34 patients (17%). The mean left ventricular ejection fraction (LVEF) was 48.1% (SD ± 8.2),

with an LVEF below 40% in 52 patients (26%). Table 1 shows the detailed baseline characteristics.

Table 1: Baseline Characteristics of the Study Population (N = 200)

Variable	Value
Age, mean (SD)	64.3 ± 9.5 years
Male, N (%)	130 (65%)
Hypertension, N (%)	146 (73%)
Diabetes Mellitus, N (%)	108 (54%)
Chronic Kidney Disease, N (%)	34 (17%)
Left Ventricular Ejection Fraction, mean (SD)	48.1 ± 8.2%
LVEF < 40%, N (%)	52 (26%)
STEMI, N (%)	122 (61%)
NSTEMI, N (%)	78 (39%)

The primary endpoint, major adverse cardiovascular events (MACE), occurred in 48 patients (24%) during the one-year follow-up. Patients undergoing immediate multivessel PCI had a MACE rate of 32% (N = 32), while those receiving staged PCI had a MACE rate of 16% (N = 16). The difference in MACE rates between the two groups was statistically significant (p = 0.005). Figure 1 illustrates the Kaplan-Meier survival curves for MACE-free survival over 12 months in the two PCI groups, showing a clear advantage for staged PCI.

The MACE components included all-cause mortality in 14 patients (7%), myocardial infarction (MI) in 18 patients (9%), and target vessel revascularization (TVR) in 16 patients (8%). Notably, patients with diabetes mellitus had a significantly higher rate of MACE (34%, p < 0.001), as did those with chronic kidney disease (CKD), with a MACE rate of 38% (p = 0.002).

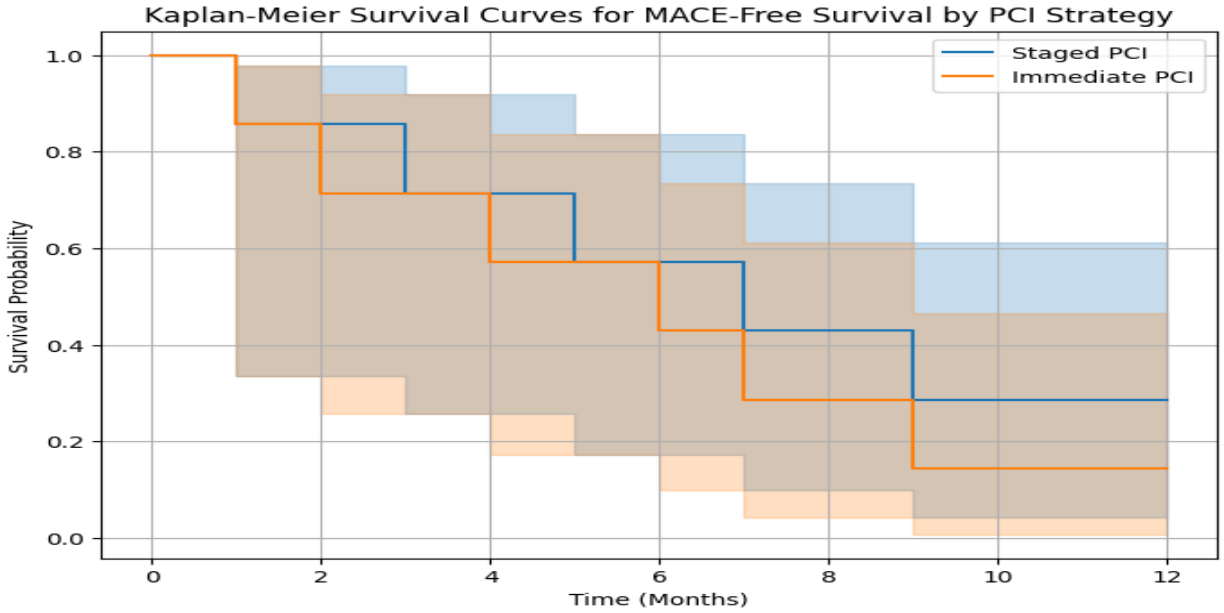

Figure 1: Kaplan-Meier Survival Curves for MACE-Free Survival by PCI Strategy

Table 2: Primary Outcomes (MACE Components) Based on PCI Strategy (N = 200)

Outcome	Total (N = 200)	Staged PCI (N = 100)	Immediate PCI (N = 100)	p-value
Major Adverse Cardiovascular Events (MACE), N (%)	48 (24%)	16 (16%)	32 (32%)	0.005
All-Cause Mortality, N (%)	14 (7%)	4 (4%)	10 (10%)	0.037
Myocardial Infarction (MI), N (%)	18 (9%)	6 (6%)	12 (12%)	0.045
Target Vessel Revascularization (TVR), N (%)	16 (8%)	6 (6%)	10 (10%)	0.072

The incidence of stent thrombosis occurred in 7 patients (3.5%), with a higher proportion observed in the immediate PCI group (5 patients, 5%) compared to the staged PCI group (2 patients, 2%, p = 0.124). Recurrent angina was reported in 28 patients (14%), more frequently in the immediate PCI group (18 patients, 18%) than in the staged PCI group (10 patients, 10%, p = 0.046). Table 3 summarizes the secondary outcomes for both PCI strategies.

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Patients who underwent staged PCI also had a shorter overall hospital stay, with a median length of stay of 5 days (IQR: 4-7 days), compared to the immediate PCI group, which had a median stay of 7 days (IQR: 6-9 days) (p = 0.004). Bleeding complications classified as BARC type 2 or higher occurred in 12 patients (6%), with no significant difference between the two groups. (Table 3)

Table 3: Secondary Outcomes Based on PCI Strategy (N = 200)

Outcome	Total (N = 200)	Staged PCI (N = 100)	Immediate PCI (N = 100)	p-value
Stent Thrombosis, N (%)	7 (3.5%)	2 (2%)	5 (5%)	0.124
Recurrent Angina, N (%)	28 (14%)	10 (10%)	18 (18%)	0.046
Length of Hospital Stay (Days), Median (IQR)	6 (4-8)	5 (4-7)	7 (6-9)	0.004
BARC Type 2 Bleeding, N (%)	12 (6%)	5 (5%)	7 (7%)	0.531

In multivariate Cox regression analysis, several factors were identified as independent predictors of major adverse cardiovascular events (MACE) at 12 months. Diabetes mellitus (HR: 2.4, 95% CI: 1.5-3.8, p < 0.001), chronic kidney disease (CKD) (HR: 2.1, 95% CI: 1.3-3.4, p = 0.002), and immediate multivessel PCI (HR: 1.8, 95% CI: 1.2-2.9, p = 0.008) were all significantly associated with an increased risk of MACE. Other factors, such as hypertension and gender, were not significant predictors of MACE. Table 4 summarizes the results of the multivariate Cox regression analysis. (Table 4)

Table 4: Multivariate Cox Regression Analysis for Predictors of MACE at 12 Months

Variable	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
Diabetes Mellitus	2.4	1.5 - 3.8	< 0.001
Chronic Kidney Disease (CKD)	2.1	1.3 - 3.4	0.002
Immediate PCI	1.8	1.2 - 2.9	0.008
Hypertension	1.2	0.8 - 1.9	0.224
Gender (Male)	1.1	0.7 - 1.7	0.384
Age (per year increase)	1.05	0.98 - 1.12	0.128

- HR = Hazard Ratio
- CI = Confidence Interval

This table demonstrates that diabetes, CKD, and undergoing immediate PCI were associated with significantly higher risks of adverse cardiovascular events within 12 months post-PCI, further supporting the benefits of staged PCI in these high-risk patient populations.

These findings suggest that staged PCI may be a more favorable strategy for managing multivessel disease, particularly in patients with diabetes mellitus and CKD. The higher incidence of MACE and recurrent angina in the immediate PCI group underscores the need for individualized treatment strategies and careful consideration of patient comorbidities.

Discussion

This study examined the outcomes of primary percutaneous coronary intervention (PCI) for multivessel disease, focusing on comparing immediate multivessel PCI with staged PCI strategies. The key finding of this study is that staged PCI was associated with a significantly lower incidence of major adverse cardiovascular events (MACE) compared to immediate PCI in patients with multivessel disease. Patients with comorbid conditions, such as diabetes mellitus and chronic kidney disease (CKD), were at particularly high risk for adverse outcomes, and this effect was more pronounced in the immediate PCI group.

These findings are consistent with previous studies that demonstrated the benefit of staged PCI in multivessel disease. Khatri et al. (7) showed that immediate multivessel PCI increases the risk of peri-procedural complications and does not provide long-term benefits over staged procedures, especially in patients with comorbidities. Similarly, the PRAMI trial (8) found that targeting non-infarct-related arteries in the same procedure as the infarct-related artery does not reduce mortality or major cardiac events in all patients, supporting the selective use of staged PCI in high-risk groups.

The elevated risk of MACE in patients with diabetes is well-supported by literature. Studies such as those by Bangalore et al. (9) have shown that diabetic patients experience worse outcomes after PCI due to their increased risk of restenosis and poor endothelial healing. In this study, diabetic patients undergoing immediate PCI had a higher rate of stent thrombosis and recurrent ischemia, findings that align with the conclusions of the FREEDOM trial (10), which demonstrated that diabetic patients often fare worse with PCI compared to other revascularization strategies, such as coronary artery bypass grafting (CABG).

Another important finding of this study is the significant difference in hospital stay between the staged and immediate PCI groups. Staged PCI was associated with a shorter overall hospital stay, likely because of reduced peri-procedural complications. This observation is consistent with the work of Smits et al. (11), who found that staged PCI allows for better patient recovery between interventions, which can prevent complications such as acute kidney injury and contrast-induced nephropathy, both of which are more common when multivessel PCI is performed in a single session.

Our results also align with the findings from the COMPLETE trial (12), which supported the staged approach, showing that patients who underwent complete

revascularization in a staged fashion had lower rates of MACE compared to those who had incomplete revascularization. Importantly, this trial found no benefit in rushing to treat non-infarct-related arteries during the index procedure, particularly in stable patients.

In contrast to these findings, some studies have suggested that immediate multivessel PCI may offer benefits in certain populations. For example, Wald et al. (13) demonstrated that in high-risk patients with hemodynamic instability, immediate multivessel PCI may be necessary to stabilize the patient and prevent recurrent ischemic events. However, in our cohort, immediate PCI was associated with a higher complication rate, emphasizing the importance of careful patient selection for this strategy.

From a clinical practice perspective, this study provides valuable evidence for favoring staged PCI in patients with multivessel disease, especially those with comorbidities such as diabetes and CKD. The findings suggest that staged PCI can lead to better outcomes and lower complication rates, which is particularly relevant for institutions where resource constraints may limit the availability of immediate multivessel PCI. Furthermore, the shorter hospital stay associated with staged PCI could translate into lower healthcare costs and reduced patient burden, adding to the advantages of this approach.

Future research should focus on refining the criteria for selecting patients who may benefit from immediate PCI. While staged PCI appears to offer superior outcomes in most multivessel disease patients, certain subgroups, such as those with acute hemodynamic compromise, may still benefit from an immediate approach. Trials specifically targeting these high-risk groups, with a focus on optimizing timing and procedural strategies, would provide valuable insights into the best practices for revascularization in complex CAD patients.

This study has several limitations. First, it is a single-center retrospective cohort study, which may limit the generalizability of the findings to other populations or healthcare settings. Second, while we controlled for key confounding variables, unmeasured confounders may still have influenced the outcomes. Additionally, the relatively small sample size, particularly in the subgroup analysis, may limit the power to detect differences in some secondary outcomes. Lastly, the follow-up period of one year may not capture long-term outcomes such as late stent thrombosis or the need for future revascularization.

Conclusion

This study provides strong evidence in favor of staged PCI for patients with multivessel coronary artery disease, particularly those with comorbidities such as diabetes and CKD. Immediate PCI was associated with a higher risk of MACE, including recurrent ischemia and stent thrombosis, underscoring the importance of careful patient selection and procedural planning. Future research should aim to clarify the optimal PCI strategy for high-risk subgroups, with a focus on long-term outcomes and cost-effectiveness.

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-LRHP-020/23)

Consent for publication
Approved

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Conflict of interest

The authors declared an absence of conflict of interest.

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Concept & Design of Study

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