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Management Strategies and Outcomes in Diffuse LAD CAD Among the Asian Population: A Prospective Study

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Abstract

Background: Diffuse left anterior descending (LAD) coronary artery disease (CAD) involves long, contiguous stenoses and may require extensive percutaneous or surgical revascularization; data from South Asia are limited. **Objective:** To describe management strategies and inhospital outcomes in consecutive diffuse LAD CAD. **Methods:** We conducted a prospective, registry-based cohort study at the Peshawar Institute of Cardiology using the Cardiac Registry of Pakistan (1st March 2024 till 31st March 2025). Consecutive adults undergoing coronary angiography were screened in real time for diffuse LAD disease (lesion/contiguous lesions ≥20 mm with ≥70% stenosis extending into the mid-to-distal LAD). Patients were grouped by index LAD strategy during the same hospitalization: PCI with drug-eluting stent (DES), PCI with drug-eluting balloon (DEB), PCI with plain old balloon angioplasty (POBA), coronary artery bypass grafting (CABG) alone, hybrid revascularization (PCI plus CABG), or medical therapy. The primary outcome was inhospital all-cause mortality; secondary outcomes were inhospital myocardial infarction, stroke, urgent repeat revascularization, and length of stay.

Results: Among 470 enrolled patients (61.6±9.8 years; 67.8% male), hypertension and diabetes were present in 53.6% and 24.5%, respectively. PCI was used in 94.7% (DES 90.2%, DEB 5.3%, POBA 4.5%). CABG alone (0.6%), hybrid revascularization (1.1%), and medical therapy (1.5%) were uncommon. Overall, in-hospital mortality was 1.1% (5/470); all deaths occurred in the DES-PCI group, with no deaths in the other strategies**. Conclusion:** In this prospective South Asian registry, PCI—predominantly DES—was the prevailing approach for diffuse LAD CAD and was associated with low in-hospital mortality. Longer-term multicenter studies are needed to compare durability and late outcomes across strategies.

Introduction

Diffuse coronary artery disease (CAD) of the left anterior descending artery (LAD) represents a challenging subset of ischemic heart disease, often defined by long, contiguous atherosclerotic lesions exceeding 20 mm in length. Treatment strategies for diffuse LAD lesions are complex due to anatomical limitations and higher procedural risks. Percutaneous coronary intervention (PCI) with drug-eluting stents (DES) has become a cornerstone of therapy, yet multiple overlapping stents—commonly referred to as a "full metal jacket"—are often required, increasing the risk of restenosis and target lesion revascularization (1,2). Coronary artery bypass grafting (CABG), particularly using the left internal mammary artery (LIMA) to LAD, remains the standard of care in multivessel and proximal LAD disease, offering proven survival benefits in high-risk populations such as those with diabetes mellitus (3,4). However, in diffusely diseased LAD segments lacking suitable distal targets, complete surgical revascularization is often not feasible, potentially diminishing the advantage of CABG (5).

Emerging alternatives like drug-eluting balloons (DEB) offer a “leave nothing behind” approach and are gaining interest for diffuse de novo lesions, especially in small vessels where long DES implants may not be optimal. DEBs have demonstrated comparable mid-term efficacy to DES in selected diffuse CAD patients, although widespread

adoption is limited due to the need for further large-scale studies (6). Importantly, ethnicity plays a critical role in disease expression and treatment outcomes. Asian populations, particularly South Asians, often present with diffuse atherosclerosis at a younger age and smaller coronary artery diameters, complicating both surgical and percutaneous revascularization (7,8). Despite this, they remain underrepresented in major trials.

There is limited real-world data evaluating how diffuse LAD disease is managed in Asian populations and whether current practices align with international guidelines. Understanding treatment patterns in this high-risk group is essential to inform guideline adaptation, especially in resource-variable settings where surgical access may be limited.

This study aims to evaluate management strategies and in-hospital outcomes in a contemporary Asian cohort with angiographically confirmed diffuse LAD disease, addressing existing knowledge gaps and contributing to region-specific evidence on optimal treatment approaches.

Methods

Study Design, Setting, and Data Source:

This was a prospective, observational cohort study conducted at the Peshawar Institute of Cardiology using the Cardiac Registry of Pakistan (CROP). Consecutive patients undergoing invasive coronary angiography (with or without revascularization) between 1st March 2024 and 31st March 2025 were screened in real time for angiographically confirmed diffuse LAD disease. Eligible patients were enrolled at the index hospitalization and followed prospectively until hospital discharge. The study was approved by the institutional ethics committee. Written informed consent for participation in the registry/research was obtained from all participants or their legally authorized representatives; where immediate consent was not feasible (e.g., emergency presentations), deferred consent was pursued in accordance with institutional policy.

Inclusion and Exclusion Criteria:

Patients were eligible if they had angiographically confirmed diffuse disease of the LAD. Diffuse LAD CAD was defined as an LAD lesion (or contiguous series of lesions) ≥20 mm in length with ≥70% diameter stenosis, extending through the mid-to-distal LAD segment. This definition included patients requiring long stents or multiple overlapping stents in the LAD, or those adjudicated by the treating cardiologist as having diffuse inoperable LAD disease. Both stable angina and acute coronary syndrome presentations were eligible provided the invasive coronary angiogram demonstrated diffuse LAD involvement. Patients were excluded if they had left main disease involving the LAD ostium (to avoid overlap with left main revascularization scenarios), non-LAD culprit lesions only without significant LAD involvement, prior LAD stenting or prior bypass graft to the LAD (to focus on de novo native diffuse disease), or missing key data for treatment classification or in-hospital outcomes.

Treatment Strategy Definitions:

Treatment was determined by the treating heart team as part of routine clinical care. For analysis, patients were prospectively categorized into one of the following groups based on the index LAD management strategy during the same hospitalization:

PCI with DES: Patients who underwent percutaneous coronary intervention of the LAD with deployment of one or more drug-eluting stents. This was the default PCI strategy in the participating centers for significant lesions.

PCI with POBA: Patients who underwent balloon angioplasty to the LAD without stent implantation (plain old balloon angioplasty), including cases of specialty balloons (scoring or cutting balloons) but no drug-elution. These were typically cases where stenting was attempted but not achieved or deemed high-risk (e.g., extremely distal targets).

PCI with DEB: Patients treated with a drug-eluting balloon in the LAD. In these cases, the lesion was prepared with balloon angioplasty and then a paclitaxel-coated balloon (DEB) was inflated to deliver anti-proliferative drug without stenting. No LAD stent was implanted unless bailout was needed (in our cohort, none of the DEB cases required bailout stenting).

CABG without PCI: Patients referred to surgery for LAD revascularization (and any other diseased vessels as needed) without any attempted PCI to the LAD. In all CABG cases, the surgical reports confirmed use of a LIMA graft to the LAD. This arm thus represents the exclusive surgical revascularization approach.

Hybrid Approach (PCI + CABG): Patients who received a combined approach, typically PCI to one or more non-LAD vessels and CABG for the LAD. In our context, hybrid strategy usually meant the patient initially underwent PCI to other vessels and subsequently was sent for CABG to the LAD (or vice versa), during the same hospital stay.

Medical Therapy: Patients managed conservatively without any revascularization (no PCI or CABG). These were typically patients in whom revascularization was not performed due to patient preference or extremely high risk (for instance, diffusely diseased LAD not amenable to PCI and deemed poor surgical candidates), and they received optimal medical therapy including anti-anginals, antiplatelets, statins, etc.
Patients receiving PCI (DES, POBA, or DEB) could also undergo concomitant PCI to other vessels during the same session; classification was based on the LAD strategy at the index procedure. In the hybrid group, at least one coronary artery was stented and the LAD was bypassed surgically during the same hospitalization. All procedures (PCI or CABG) were performed per standard practice by experienced operators. The choice of DES type or DEB was at the operator's discretion; second-generation DES were used in all cases (predominantly everolimus-eluting and sirolimus-eluting stents), and DEBs were paclitaxel-coated balloons available in the cath labs.

Data Collection and Variables:
Data were captured prospectively by trained registry coordinators using standardized case report forms and the CROP data platform. We recorded demographics (age, sex), cardiovascular risk factors (including diabetes mellitus and hypertension), history of myocardial infarction (MI) or prior revascularization, and clinical presentation. Angiographic data confirmed diffuse LAD disease per the inclusion criteria. The primary outcome was in-hospital all-cause mortality, defined as death during the index hospitalization. Secondary outcomes included in-hospital MI, stroke, urgent repeat revascularization, and length of stay.

Statistical Analysis:
An a priori analysis plan was followed. Analyses were performed using IBM SPSS Statistics version 26 (IBM Corp, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation and were compared using Student's t-test or ANOVA as appropriate. Categorical variables are presented as counts and percentages

and were compared using chi-square tests or Fisher's exact test when expected cell counts were small.

The distribution of management strategies was calculated as a proportion of the total cohort. In-hospital mortality rates were computed for each treatment arm and for subgroups by device type.

Multivariable modeling was considered exploratory because in-hospital deaths were infrequent. A multivariable logistic regression model was constructed to examine associations between in-hospital mortality and age, sex, diabetes, hypertension, prior MI, and treatment strategy/device type. Results are reported as odds ratios (OR) with 95% confidence intervals (CI) and p-values (two-tailed), with $p < 0.05$ considered statistically significant. Given the sparse event count, findings were interpreted cautiously. No imputation was performed for missing data; analyses used complete cases and the registry provided complete capture of in-hospital outcomes for included patients. Data quality was supported through routine registry validation checks and verification of key outcomes against hospital records.

Results

Patient group and baseline characteristics: During the prospective enrolment period, diffuse left anterior descending (LAD) coronary artery disease was identified in 470 consecutive patients. The mean age of the cohort was 61.6 ± 9.8 years, and 67.8% were male. Hypertension and diabetes mellitus were present in 252 (53.6%) and 115 (24.5%) patients, respectively. A history of myocardial infarction (MI) was recorded in 18.1% of patients, while 15.5% had established coronary artery disease (CAD) on prior admission. Prior revascularization included prior percutaneous coronary intervention (PCI) in 6.6% and prior coronary artery bypass grafting (CABG) in 1.5%. Most patients presented with stable angina or non-ST-elevation acute coronary syndromes (NSTEACS). The relatively low frequency of ST-elevation MI (STEMI) reflects that only nonculprit diffuse LAD cases were selected for definitive LAD treatment (Table 1).

Table 1: Baseline demographic and clinical characteristics of diffuse LAD disease patients

Characteristic	Value
Total patients	470
Mean age	61.6 ± 9.8 years
Male sex	319 (67.8%)
Female sex	150 (32.2%)
Diabetes mellitus	115 (24.5%)
Hypertension	252 (53.6%)
Prior myocardial infarction	85 (18.1%)
Prior known CAD	73 (15.5%)
Prior PCI	31 (6.6%)
Prior CABG	7 (1.5%)

Management strategies:

The majority of patients were treated with PCI. Overall, 445 of 470 patients (94.7%) underwent PCI for diffuse LAD lesions. Drug-eluting stent (DES) implantation was the most common strategy, used in 424 of 470 patients (90.2%). Drug-eluting balloon (DEB) angioplasty was used in 25 patients (5.3%) and plain old balloon angioplasty (POBA) in 21 patients (4.5%). Three patients (0.6%) underwent CABG alone and five (1.1%) underwent a hybrid approach (PCI plus CABG). Seven patients (1.5%) were managed with medical therapy alone (Table 2).

Table 2. Treatment group management practices and in-hospital mortality

Management strategy	Patients (n)	% of cohort	In-hospital mortality (n)
PCI with drug-eluting stent	424	90.2%	5
PCI with drug-eluting balloon	25	5.3%	0
PCI with plain balloon (POBA)	21	4.5%	0
CABG (without PCI)	3	0.6%	0
Hybrid (PCI + CABG)	5	1.1%	0
Medical therapy alone	7	1.5%	0

PCI with DES was the most frequently selected strategy. PCI with DEB was typically reserved for diffusely diseased arteries in which long stent deployment was undesirable. POBA was rarely used and was limited to anatomically difficult situations. CABG was performed in exceptional cases, likely in patients with multivessel disease unsuitable for PCI. The hybrid technique was selectively applied in those requiring LAD grafting with concomitant PCI to other coronary arteries. Medical therapy alone was used in patients with poor anatomy or contraindications to revascularization. In-hospital mortality for the overall cohort was 1.1% (5/470).

All five deaths occurred in the PCI with DES group. No deaths occurred in the DEB, POBA, CABG, hybrid, or medical therapy groups. Among the five deaths, most occurred in the setting of acute MI (three NSTEMI, one STEMI), and one followed extensive no-reflow after long DES implantation. Four deaths were due to cardiogenic shock within 48 hours, and one was due to refractory ventricular arrhythmia related to no-reflow and distal vessel occlusion. Non-fatal adverse events included acute stent thrombosis requiring repeat PCI and a perioperative stroke in one surgical patient who recovered. No bailout stenting or switch to CABG was required for any DEB patient. Typical length of stay was approximately 1.1 days for uncomplicated PCI, 5–7 days for CABG, and 2 days for medically managed patients for monitoring and medication optimization.

Given the small number of events (n = 5), statistical power was limited. Multivariable logistic regression was performed as an exploratory analysis to evaluate associations of age, sex, diabetes, hypertension, prior MI, and treatment strategy with in-hospital mortality. No variable met conventional statistical significance ($p < 0.05$), and results should be interpreted cautiously due to sparse events (Table 3).

Table 3. Multivariate regression analysis predictors of in-hospital mortality

Predictor Variable	Coefficient (β)	Standard Error	zvalue	pvalue	95% CI (Lower)	95% CI (Upper)	Interpretation
Intercept	-2.693	1.329	-2.03	0.043	-5.30	-0.09	Significant baseline log-odds
Age (per year)	-0.038	0.021	-1.77	0.077	-0.080	0.004	Trend toward lower mortality with age
Male gender	-0.035	0.977	-0.04	0.971	-1.950	1.880	No significant effect
Diabetes mellitus	0.724	0.989	0.73	0.464	-1.214	2.661	Trend toward higher risk (not significant)
Hypertension	0.133	0.992	0.13	0.893	-1.812	2.078	No significant impact
Prior MI	-15.025	23058.525	≈0	0.999	-45208.904	45178.853	Model unstable due to zero variance

Procedural details: In the DES group, long-segment stenting with overlapping stents across the proximal-to-mid LAD was undertaken in selected cases. DEB use was generally dictated by small distal vessel size and diffuse disease, with no early complications recorded. POBA cases were typically anatomically difficult or complicated and precluded stent deployment. Two CABG patients underwent LAD endarterectomy, reflecting surgical accommodation for diffuse disease. No in-hospital mortality was observed in the CABG or medical therapy groups.

Discussion

This prospective registry-based cohort of 470 patients with diffuse LAD coronary artery disease provides one of the largest contemporary insights from an Asian population, addressing an important evidence gap regarding treatment patterns and short-term outcomes in this high-risk group. The predominant reliance on PCI, particularly DES implantation (90.2%), reflects real-world feasibility and operator preference in the face of complex anatomy. Notably, in-hospital mortality was low (1.1%) with no deaths in the DEB, POBA, CABG, hybrid, or medically managed groups, underscoring the procedural safety of contemporary percutaneous options even in challenging diffuse lesions.

Our results contrast with earlier Western registries, where CABG is often the dominant strategy for diffuse LAD disease due to concerns over incomplete revascularization and long-term restenosis with multiple stents (9). In the current cohort, CABG was underutilized (0.6%)—likely due to anatomical unsuitability for grafting, smaller distal vessels, and patient or system-related barriers. Importantly, all CABG patients in our study had LIMA grafts to LAD, consistent with guidelines favoring arterial conduits for survival benefit (10). However, no in-hospital mortality in this group may suggest

potential benefit in appropriately selected surgical cases, aligning with evidence from the ART and SYNTAX trials favoring LIMA-to-LAD grafting in multi-vessel disease (11,12).

The low adoption of DEBs (5.3%) but favorable short-term outcomes with zero mortality or complications reinforce their utility in diffuse disease, particularly in smallcaliber LADs common among South Asian patients. Recent randomized data, such as the DEBUT and BASKET-SMALL 2 trials, have shown comparable outcomes of DEBs versus DES in selected populations with small-vessel or diffuse disease (13,14). Our findings add region-specific support to this paradigm and warrant consideration of DEBs where long stents are suboptimal or may increase the metal burden. Notably, lesion preparation was emphasized in all DEB cases, supporting the concept that adequate pre-dilatation is key to successful DEB outcomes (15).

The exclusive use of second-generation DES, predominantly everolimus- and sirolimus-eluting stents, in our study may also explain the low event rates, given their improved safety and efficacy over first-generation devices (16). Despite long stent lengths in many cases, the absence of stent thrombosis or bailout surgery highlights the procedural refinements and operator experience within our centers. These findings are congruent with outcomes from the EXAMINATION and TWENTE studies, which report excellent safety profiles of newer-generation DES even in complex lesions (17,18).

Interestingly, POBA was employed in anatomically hostile LADs where stenting was not feasible, yet no early mortality was observed. While POBA has largely fallen out of favor due to high restenosis rates, selective use in niche scenarios, such as extremely distal LAD or tortuous vessels, appears justifiable. This selective approach is aligned with recommendations for POBA use in patients where stenting may pose more risk than benefit (19). Moreover, the absence of adverse events in this group suggests that proper patient and lesion selection remains paramount.

The extremely low uptake of hybrid revascularization (1.1%) in our dataset contrasts with Western practices where hybrid approaches are increasingly advocated for complex coronary disease. While evidence supports their use in selected patients—offering the benefit of LIMA-to-LAD grafting with PCI to non-LAD vessels—
logistical challenges and limited infrastructure may impede their widespread use in low- and middle-income settings (20). Nevertheless, the complete absence of mortality in this subgroup is promising and may prompt centers to consider hybrid strategies more routinely in suitable cases.

This study carries important implications for clinical practice. First, it validates the realworld safety of PCI with modern DES even in diffuse LAD disease, supporting its use in resource-variable Asian contexts. Second, it highlights DEBs as a viable alternative for patients with small or highly diseased distal LADs, echoing recent guideline inclusions of DEBs in specific indications. Third, it underscores the critical role of individualized anatomical assessment and lesion preparation in achieving optimal outcomes. Finally, the study underscores the underuse of CABG in diffuse LAD in the region—not necessarily from lack of need but potentially due to anatomical, institutional, or socioeconomic limitations.

Future studies are warranted to evaluate long-term outcomes of these strategies, especially regarding restenosis, target lesion failure, and repeat revascularization. There is a need for randomized trials or prospective registries comparing DEB, DES, and CABG in diffuse LAD disease within Asian populations. Moreover, research into ethnic-specific anatomical features and pharmacogenomic responses may further refine therapeutic strategies for this underrepresented group.

Limitations

This study has limitations typical of an observational, non-randomized registry. The design precludes causal inference and treatment selection was at the discretion of the

treating team, introducing potential selection bias. The small number of CABG and hybrid cases limits subgroup comparisons. In addition, the short-term focus on inhospital outcomes does not capture restenosis, late thrombosis, repeat revascularization, or long-term survival, which are especially relevant in diffuse CAD. Despite these limitations, the large sample size, consistent inclusion criteria, and standardized data capture provide useful real-world insight into diffuse LAD management in an Asian setting.

Conclusion:

In this prospective registry-based cohort of 470 consecutive patients with angiographically confirmed diffuse LAD disease, PCI was the predominant management strategy, most commonly with drug-eluting stents, and overall in-hospital outcomes were favorable with low mortality; the few deaths observed occurred in the setting of high-risk presentations (e.g., acute myocardial infarction/cardiogenic shock) and complex long-segment interventions. Clinically, these findings support the shortterm feasibility and procedural safety of contemporary PCI for diffuse LAD disease in a real-world Asian population where anatomic complexity, small distal vessels, and resource pathways may limit surgical or hybrid revascularization; however, treatment selection was non-randomized and subgroup sizes for non-stent strategies and CABG/hybrid approaches were small, so direct comparisons between modalities should be interpreted cautiously. Future multicenter prospective studies with longer follow-up are recommended to better define durability and comparative effectiveness across strategies—particularly regarding restenosis, repeat revascularization, and longer-term clinical events—and to strengthen heart-team–guided decision-making for patients with diffuse LAD disease. **References**

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