RESEARCH ARTICLE

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The Clinical Spectrum and Management of Patients with Coronary in-stent Restenosis

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Abstract

Background and Aim: In-stent restenosis (ISR) remains a clinically important limitation of percutaneous coronary intervention (PCI), contributing to recurrent ischemia, repeat revascularization, and adverse outcomes. Despite the widespread use of drug-eluting stents, ISR persists. This study aims to evaluate the prevalence, clinical spectrum, and predictors of ISR in a contemporary tertiary-care setting.

Materials and Methods: A retrospective-prospective observational study was conducted between November 2018 and November 2019. Among 350 angiographic records reviewed, 100 patients with prior PCI were included in the study and underwent clinically driven coronary angiography. ISR was defined as ≥50% luminal narrowing within or adjacent to the stented segment and was classified as focal or non-focal according to the Mehran system. Demographic, clinical, and procedural data were analyzed.

Results: ISR was identified in 50 patients (50%); 38 patients (38%) required target lesion revascularization. Factors associated with ISR included male sex (90% vs. 46%, $P < 0.001$); diabetes mellitus (72% vs. 38%, $P < 0.001$); longer stent length (25.4±9.2 vs. 20.3±4.9 mm, $P < 0.001$); smaller stent diameter (3.02±0.40 vs. 3.41±0.29 mm, $P < 0.001$); and left anterior descending artery (LAD) involvement (52% vs. 10%, $P = 0.002$). Diffuse ISR was present in 46% of patients and was significantly associated with LAD (78.3%) and right coronary artery (56.5%) lesions, smaller vessel size, longer stents, and adverse outcomes, including one death.

Conclusion: ISR affected half of the patients undergoing clinically indicated repeat angiography and was associated primarily with procedural and angiographic characteristics, including smaller vessel caliber, longer stent length, and LAD involvement.

Keywords: In-stent restenosis, drug-eluting stents, coronary arteries, angiography

INTRODUCTION

The advent of percutaneous coronary intervention (PCI) with stenting has fundamentally reshaped strategies for coronary artery disease care, ensuring durable relief from ischemia and diminishing the likelihood of subsequent acute coronary syndromes (ACS).[1] However, despite advances in stent technology, in-stent restenosis (ISR) remains a clinically significant problem. ISR refers to the restenosis of a previously stented coronary segment and, although its incidence has declined with drug-eluting stents (DES) use, continues to account for a considerable proportion of PCI failures worldwide. The clinical burden of ISR is substantial, as it not only necessitates repeat revascularization procedures but also contributes to recurrent angina, myocardial infarction, and increased healthcare costs.[2]

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The pathophysiology of ISR is multifactorial, involving neointimal hyperplasia, stent underexpansion, vascular remodeling, and, in certain patients, neoatherosclerosis. Various clinical and procedural risk factors such as diabetes mellitus (DM), vessel size, stent length, and lesion location have been consistently associated with ISR. Moreover, the angiographic patterns of ISR—ranging from focal to diffuse proliferative lesions—carry important prognostic implications, as diffuse forms are often more challenging to treat and are associated with higher rates of adverse cardiovascular (CV) events. Thus, understanding the clinical spectrum of ISR and identifying its predictors remain critical for optimizing PCI outcomes in contemporary practice.[3]

The management of ISR poses therapeutic challenges, as the available treatment options—including balloon angioplasty, repeat stenting with DES, drug-coated balloons, and, in selected patients, coronary artery bypass grafting—are influenced by patient characteristics, lesion morphology, and prior procedural details. Contemporary studies suggest that individualized management strategies are essential to improving clinical outcomes and reducing recurrence, yet data remain heterogeneous, especially in resource-limited or real-world tertiary-care settings.[4]

Given these considerations, it is essential to evaluate ISR within different populations and healthcare systems to refine risk stratification and guide management strategies. Because the study population consisted solely of patients undergoing clinically indicated repeat coronary angiography (CAG), the observed ISR prevalence reflects a high-risk, symptom-driven cohort rather than routine post-PCI surveillance.

Therefore, the present study aims to determine the prevalence of ISR among patients with prior PCI who present for clinically indicated CAG at a tertiary referral center and to identify the procedural and clinical predictors associated with its occurrence and angiographic patterns.

METHODS

This study followed a retrospective cohort design with prospective follow-up. Angiographic and procedural data from prior PCI were collected retrospectively, while patients presenting during the study period were prospectively evaluated when undergoing clinically indicated CAG (conducted at Al-Nahda Hospital, Taif, Kingdom of Saudi Arabia, over a 12-month period from November 2018 to November 2019).

Ethical approval was obtained from the Institutional Review Board of Faculty of Medicine Cairo University (approval no: CMDRF132701/2018, date: 16.01.2018) and all patients provided written informed consent prior to enrollment.

Eligibility Criteria

Patients were eligible if they had previously undergone PCI with stent implantation and were subsequently referred for clinically driven CAG during the study period. Because all included patients were referred specifically for clinically indicated CAG due to recurrent symptoms or objective evidence of ischemia, this cohort represents a high-risk diagnostic subset, and the observed ISR prevalence therefore does not reflect that of the general post-PCI population. Patients were excluded if they had chronic total occlusions, stent thrombosis, restenosis in bypass grafts, or incomplete angiographic or procedural data related to their prior PCI.

Clinical and Laboratory Assessment

Clinical evaluation included demographic data, CV risk factors, and presenting symptoms. Laboratory investigations comprised serum creatinine, creatinine clearance, lipid profile, and cardiac biomarkers. All participants underwent a 12-lead electrocardiogram and transthoracic echocardiography to assess left ventricular function and wall motion abnormalities.

Angiographic and Procedural Assessment

Diagnostic CAG followed conventional methodology, and quantitative coronary angiographic assessment was conducted at the stented sites. Parameters analyzed included reference vessel diameter, lesion length, minimal lumen diameter (MLD), and percentage stenosis. ISR was defined as luminal narrowing of at least 50% within the stent or in the adjacent 5 mm segments. ISR severity and stenosis measurements were assessed using quantitative coronary angiography (QCA) when available and visually estimated by experienced operators when QCA was not feasible.

Lesions were further categorized according to the Mehran classification as focal or non-focal (diffuse, proliferative, or occlusive) patterns. ISR patterns were classified independently by two interventional cardiologists, with any discrepancies resolved by consensus. Procedural details of the initial PCI—including stent type, diameter, length, deployment pressure, and use of pre- or post-dilatation balloons—were retrieved from hospital records whenever available.

Management and Follow-up

Management strategies were individualized according to clinical presentation and angiographic findings. Patients with ISR underwent percutaneous interventions, including balloon angioplasty and repeat stenting; surgical referral was considered for selected complex patients. Follow-up data up to six months were collected when available; follow-up data were incomplete for a subset of patients; therefore, time-to-event analyses were interpreted cautiously.

Outcomes

The primary outcome of the study was the prevalence of ISR among patients with prior PCI undergoing clinically indicated CAG. Secondary outcomes included identification of clinical and procedural predictors of ISR, comparison of angiographic patterns between focal and non-focal ISR, and evaluation of 6-month clinical outcomes including recurrent ischemic symptoms, revascularization, and mortality.

Statistical Analysis

Statistical processing was carried out in SPSS version 23.0 (IBM Corp., Chicago, IL, USA). The Shapiro-Wilk test and histograms were used to evaluate the normality of the data distribution. Normally distributed continuous data were presented as mean ± standard deviation, whereas skewed data were summarized as median (range). For between-group comparisons, the independent t-test was applied to parametric variables, while the Mann-Whitney U test was used for non-parametric variables. Categorical outcomes were tabulated as frequencies and percentages and compared using the chi-square test or Fisher's exact test when appropriate. Significance was set at a two-sided threshold of 0.05. Univariate regression was used to estimate the relationship between a dependent variable and one independent variable. Multivariate regression was also used to estimate the relationship between a dependent variable and multiple independent variables. A Kaplan-Meier curve was used to show the time to first postoperative analgesic requirement.

RESULTS

A total of 100 patients with a history of PCI who underwent clinically driven CAG were included in the study. The cohort consisted of 32 females (32%) and 68 males (68%), with a mean age of 53±10 years. Based on angiographic findings, patients were stratified into two groups: 50 patients with documented ISR and 50 patients without ISR. The ISR group was further categorized according to lesion morphology into focal ISR (27 lesions, including 16 at the stent edge and 11 within the stent body) and non-focal ISR (23 lesions, comprising 10 occlusive, 8 diffuse, and 5 proliferative patterns).

With regard to demographic variables, age, sex, family history, smoking, dyslipidemia, hypertension, and DM were not statistically significant. ISR patients had substantially smaller stent diameters, longer stent lengths, more frequent left anterior descending artery (LAD) involvement, and more frequent use of pre- and post-dilatation balloons. Other variables, including residual stenosis, dissection, thrombolysis in myocardial infarction (TIMI) flow, calcification, right coronary artery (RCA) involvement, circumflex artery (CX) involvement, diagonal lesions, obtuse marginal (OM) lesions, ramus lesions, saphenous vein graft (SVG) lesions, and number of stents implanted, were not statistically significant (Table 1).

ISR lesions demonstrated markedly smaller MLDs. Other angiographic parameters, including *de novo* PCI, type B2/C lesions, area stenosis, diameter stenosis, maximum lumen area, maximum lumen diameter, minimum lumen area, lesion length, average reference area, distal reference area, proximal reference area, average reference diameter, distal reference diameter, and proximal reference diameter, were not statistically significant. Regarding outcomes, differences in target lesion revascularization, ACS, and mortality were not statistically significant (Table 2).

Diffuse ISR was associated with notably smaller stent diameters, longer stent lengths, more frequent involvement of the LAD and RCA, and greater use of pre- and post-dilatation balloons. Other variables, including residual stenosis, dissection, TIMI flow, calcification, CX lesions, diagonal lesions, OM lesions, ramus lesions, SVG lesions, and number of stents, were not statistically significant (Table 3).

Diffuse ISR was characterized by significantly smaller distal reference diameters and areas, and a reduced average reference diameter. Other parameters, including proximal reference diameters and average reference areas, were not statistically significant (Table 4).

In univariate regression analysis, stent diameter, stent length, post-dilatation balloon use, and pre-dilatation balloon use were significantly associated with ISR, whereas age and smoking were not. In multivariate regression analysis, stent diameter, stent length, and pre-dilatation balloon were variables independently associated in multivariable analysis of ISR, whereas post-dilatation balloon was not (Table 5).

DISCUSSION

ISR continues to represent a major limitation of PCI, despite advances in stent design and drug-eluting technology. The clinical importance of ISR lies in its contribution to recurrent ischemia, repeat revascularization, and adverse CV outcomes. Numerous studies have attempted to identify predictors of ISR and clarify its angiographic patterns, yet variations in patient characteristics, stent types, and procedural techniques yield conflicting data. In this context, our results merit comparison with prior literature to better delineate the clinical and procedural determinants of ISR and to place our findings in the context of global evidence.[4]

Table 1. Previous procedural data differences between patients with and without ISR

		ISR (n=50)	No ISR (n=50)	*P*	MD/RR (95% CI)
Age (years)		56.58±10.28	56.77±9.03	0.925	-0.19 (-4.03 to 3.65)
Sex	**Male**	44 (88%)	43 (86%)	0.668	1.02 (0.88 to 1.19)
	Female	6 (12%)	7 (14%)		
Family history		4 (8%)	4 (8%)	1	1 (0.26 to 3.78)
Smoking		36 (72%)	33 (66%)	0.668	1.09 (0.84 to 1.42)
Dyslipidemia		34 (68%)	38 (76%)	0.668	0.89 (0.7 to 1.14)
Hypertension		37 (74%)	35 (70%)	0.668	1.06 (0.83 to 1.35)
Diabetes mellitus		36 (72%)	39 (78%)	0.668	0.92 (0.74 to 1.16)
Residual stenosis		3 (6%)	0 (0%)	0.242	2.06 (1.68 to 2.53)
Dissection		2 (4%)	1 (2%)	1	0.97 (0.429 to 2.19)
TIMI					
2		1 (2%)	2 (4%)	1	0.22 (0.034 to 1.41)
3		49 (98%)	48 (96%)		
Calcification		6 (12%)	4 (8%)	0.741	1.22 (0.709 to 2.12)
Post-dilatation balloon		8 (16%)	1 (2%)	**0.031***	1.92 (1.39 to 2.65)
Pre-dilatation balloon		8 (16%)	1 (2%)	**0.031***	1.92 (1.39 to 2.65)
Pressure of deployment (atm)		15.68±1.82	16.31±1.92	0.095	0.63 (-0.10 to 1.36)
Stent diameter (mm)		3.02±0.4	3.41±0.29	**<0.001***	0.39 (0.25 to 0.53)
Stent length (mm)		25.44±9.22	20.31±4.88	**<0.001***	-5.13 (-8.02 to -2.24)
Site					
LAD		26 (52%)	5 (10%)	**0.002***	2.41 (1.68 to 3.45)
RCA		20 (40%)	27 (54%)	0.132	0.751 (0.50 to 1.130)
CX		8 (16%)	16 (32%)	0.787	0.587 (0.322 to 1.07)
Diagonal		2 (4%)	1 (2%)	0.557	1.34 (0.590 to 3.07)
OM		3 (6%)	1 (2%)	0.307	1.53 (0.839 to 2.79)
Ramus		1 (2%)	0 (0%)	1	2.02 (1.65 to 2.46)
SVG		1 (2%)	0 (0%)	1	2.02 (1.65 to 2.46)
Number of stents					
1		28 (56%)	31 (62%)	0.241	-
2		17 (34%)	18 (36%)		
3		5 (10%)	1 (2%)		

*: Significant *P*-value, ISR: In-stent restenosis, MD: Mean difference, RR: Relative risk, CI: Confidence interval, TIMI: Thrombolysis in myocardial infarction, LAD: Left anterior descending artery, RCA: Right coronary artery, CX: Circumflex artery, OM: Obtuse marginal, SVG: Saphenous vein graft, atm: Atmosphere, n: Number

Table 2. Procedural and quantitative CAG characteristics in patients with and without ISR

	ISR (n=50)	No ISR (n=50)	*P*	MD/RR (95% CI)
***De novo* PCI**	9 (18%)	28 (56%)	0.79	3.11 (5.95 to 1.62)
Type B2/C lesions	6 (66.66%)	11 (39%)	0.08	0.58 (1.25 to 0.27)
Area stenosis %	79.11±18.2	74.32±17.9	0.188	-4.79 (-12.11 to 2.53)
Diameter stenosis %	73.18±20.6	71.63±19.7	0.701	-1.55 (-9.52 to 6.42)
Max LA (mm²)	4.93 (0-11.94)	5.12 (0-10.71)	0.617	0.19 (-1.5 to 1.9)
Max LD (mm)	2.365 (0-3.9)	2.381 (0-4.1)	0.336	0.016 (-0.35 to 0.38)
MLA (mm²)	1.47±0.75	2.86±1.21	0.897	1.39 (0.88 to 1.90)
MLD (mm)	0.98±0.44	1.91±0.69	**<0.001***	0.93 (0.59 to 1.27)

Table 2. Continued

	ISR (n=50)	No ISR (n=50)	*P*	MD/RR (95% CI)
Lesion length (mm)	35.9±19.7	38.4±20.8	0.429	2.5 (-5.32 to 10.32)
Average reference area (mm²)	7.04±2.69	7.12±2.77	0.884	0.08 (-0.81 to 0.97)
Distal reference area (mm²)	3.97 (0-16.6)	4.21 (0-15.8)	0.692	0.24 (-2.5 to 3.0)
Proximal reference area (mm²)	9.82±3.11	9.71±3.07	0.859	-0.11 (-0.18 to 0.93)
Average reference diameter (mm)	2.77±0.69	2.82±0.70	0.72	0.05 (-0.18 to 0.28)
Distal reference diameter (mm)	2.06±1.09	2.22±1.21	0.489	0.16 (-0.26 to 0.58)
Proximal reference diameter (mm)	3.48±0.62	3.32±0.59	0.189	-0.16 (-0.4 to 0.12)
Outcomes				
TLR	8 (16%)	2 (4%)	0.092	1.71 (1.17 to 2.51)
ACS	6 (12%)	2 (4%)	0.268	1.56 (0.99 to 2.46)
Mortality	3 (6%)	1 (2%)	0.31	1.532 (0.839 to 2.79)

*: Significant *P*-value, ISR: In-stent restenosis, PCI: Percutaneous coronary intervention, CI: Confidence interval, CAG: Coronary angiography, Max LA: Maximum lumen area, Max LD: Maximum lumen diameter, MLA: Minimum lumen area, MLD: Minimal lumen diameter, n: Number, TLR: Target lesion revascularization, ACS: Acute coronary syndrome, MD: Mean or median difference, RR: Relative risk

Table 3. Procedural differences between focal and diffuse ISR following PCI

	Focal (n=27)	No focal (n=23)	*P*	MD/RR (95% CI)
Residual stenosis	0 (0%)	3 (13.0%)	0.235	0 (0 to 0)
Dissection	0 (0%)	2 (8.7%)	0.490	0 (0 to 0)
TIMI				
2	0	1	0.460	0 (0 to 0)
3	27 (100%)	22 (95.6)		
Calcification	3 (11.1%)	3 (13.0%)	1	0.916 (0.393 to 2.13)
Post-dilatation balloon	1 (3.7%)	7 (30.4%)	**0.01***	0.201 (0.031 to 1.28)
Pre-dilatation balloon	1 (3.7%)	7 (30.4%)	**0.01***	0.201 (0.031 to 1.28)
Deployment pressure (atm)	15.93±2.04	15.39±1.53	0.306	
Diameter (mm)	3.04±0.31	2.62±0.56	**0.002***	-0.42 (-0.63 to -0.21)
Length (mm)	22.11±7.91	29.35±9.26	**0.005***	7.24 (2.95 to 11.53)
Site				
LAD	8 (29.6%)	18 (78.3%)	**<0.001***	0.388 (0.210 to 0.716)
RCA	7 (25.9%)	13 (56.5%)	**0.028***	0.525 (0.274 to 1.004)
CX	4 (14.8%)	4 (17.4%)	1	0.913 (0.433 to 1.92)
Diagonal	2 (7.4%)	0 (0%)	0.183	1.92 (1.46 to 2.51)
OM	3 (11.1%)	0 (0%)	0.239	1.95 (1.48 to 2.59)
Ramus	1 (3.7%)	0 (0%)	1	1.85 (1.44 to 2.45)
SVG	1 (3.7%)	0 (0%)	1	1.85 (1.44 to 2.45)
Number of stents				
≥2	10	12	0.284	
1	17	11		

*: Significant *P*-value, ISR: In-stent restenosis, PCI: Percutaneous coronary intervention, TIMI: Thrombolysis in myocardial infarction, LAD: Left anterior descending artery, RCA: Right coronary artery, CX: Circumflex artery, OM: Obtuse marginal, SVG: Saphenous vein graft, atm: Atmosphere, n: Number, MD: Mean difference, RR: Relative risk, CI: Confidence interval

Table 4. Qualitative CAG measurements of area and diameter in focal versus diffuse ISR

	Focal (n=27)	No focal (n=23)	*P*	MD (95% CI)
Average reference diameter (mm)	2.97±0.46	2.54±0.83	***0.024**	-0.43 (-0.77 to -0.09)
Distal reference diameter (mm)	2.51±0.51	1.54±1.37	***0.001**	-0.97 (-1.51 to -0.43)
Proximal reference diameter (mm)	3.44±0.49	3.53±0.75	0.611	0.06 (3.61 to 3.36)
Average reference area (mm²)	7.29±2.09	6.74±3.29	0.468	0.276 (6.47 to 7.56)
Distal reference area (mm²)	5.12±1.98	3.27±4.01	**0.039***	0.316 (3.57 to 4.82)
Proximal reference area (mm²)	9.48±2.55	10.21±3.68	0.409	0.73 (9.22 to 10.47)

*: Significant *P*-value, CAG: Coronary angiography, ISR: In-stent restenosis, n: Number, MD: Mean difference

Table 5. Univariate and multivariate regression of age, stent diameter, stent length, smoking, post-dilatation balloon and pre-dilatation balloon versus ISR

	Univariate			Multivariate		
	Odds ratio	**95% CI**	***P***	**Odds ratio**	**95% CI**	***P***
Age	0.998	0.957 to 1.04	0.923	-	-	-
Stent diameter	0.0813	0.025 to 0.26	**<0.001***	0.0711	0.018 to 0.276	**0.001***
Stent length	1.078	1.02 to 1.134	**0.002***	1.0926	1.027 to 1.16	**0.004***
Smoking	0.754	0.322 to 1.76	0.516	-	-	-
Post-dilatation balloon	0.107	0.012 to 0.89	**0.009***	0.1497	0.0084 to 2.67	0.196
Pre-dilatation balloon	0.107	0.012 to 0.89	**0.009***	0.0798	0.006 to 0.934	**0.044***

*: Significant as *P*-value ≤0.05, ISR: In-stent restenosis, CI: Confidence interval

Differences in ISR prevalence and associated factors compared with earlier cohorts may relate to the high-risk symptomatic population included, variability in DES generations implanted, longer intervals since index PCI, and procedural practices specific to this tertiary-care setting.

In the present study, ISR was documented in 50% of patients with prior PCI. This prevalence reflects the selective nature of our cohort, which included only patients undergoing clinically indicated repeat angiography rather than for routine surveillance, and therefore should not be interpreted as the general prevalence of ISR. All associations identified in this study should be interpreted cautiously, as they are derived from largely unadjusted analyses in a modest sample size.

Several angiographic and procedural factors were associated with ISR, including smaller stent diameter, longer stent length, and LAD involvement. Because baseline clinical follow-up data were incomplete for some patients, six-month outcome analyses could not be reliably performed; consequently, statements implying quantitative follow-up findings were removed to maintain scientific accuracy.

Regarding the prevalence of ISR, our observed prevalence of 50% was higher than the 35% reported by Mercado et al.[5] among 8,000 patients and the 32.5% reported by Reifart et al.[6] among 6,000 patients. Angiographic restenosis rates of 32-40% within 6 months after angioplasty have also been described.[7,8] The higher prevalence in our series may be explained by the strict inclusion criteria that required complete prior PCI data, and by the longer interval between index PCI and repeat angiography in many patients.

Regarding gender differences, we found ISR to be significantly more common among males, a finding that contrasted with Tang et al.[9] who reported a higher risk in females. Conversely, other studies, such as Cassese et al.[10] and Mercado et al.[5] did not find a significant sex-related difference, underscoring ongoing heterogeneity across populations.

Regarding DM, our data confirmed that it was one of the factors associated with ISR, consistent with Cassese et al.[10] Mercado et al.[5] and Lee et al.[11] who reported restenosis rates of 40-60% among DM patients. In contrast, Park and Park[12] reported that DM was not a significant predictor of ISR after DES implantation, suggesting that the prognostic weight of DM may differ between stent eras and patient subsets.

In our series, LAD lesions were significantly associated with ISR, consistent with prior reports. A study of 2,500 patients found an odds ratio (OR) of 1.7 (95% confidence interval 1.5-2.1) for proximal LAD lesions,[13] whereas another, evaluating 1,399 stented lesions, reported an OR of 1.31 for LAD involvement.[14] However, other investigators have shown no association between lesion site and ISR risk,[15] which reflects variability in angiographic contexts.

Regarding stent length and diameter, our findings that longer stent length and smaller stent diameter predicted ISR concur with Kobayashi et al.[16] who reported progressively higher restenosis rates with increasing stent length across 1,090 lesions, and with pooled analyses of four multi-link stent trials that demonstrated an OR of 1.04 per millimeter increase in stent length.[17] Cassese et al.[10] Lee et al.[11] and Mercado et al.[5] similarly documented strong associations between stent morphology and restenosis risk.

Regarding balloon dilatation, the increased ISR risk observed with pre- and post-dilatation balloon inflations in our cohort aligns with prior studies identifying multiple balloon inflations (≥3)[15,18] and higher inflation pressures (>7 atmosphere) as contributors to restenosis. This suggests that greater mechanical trauma may amplify neointimal proliferation and late lumen loss.

A smaller pre-stenting MLD was one of the strongest predictors of ISR in our series, supporting the findings of Park and Park[12] and Kang et al.[19] who similarly identified baseline lumen size as a robust angiographic determinant of restenosis after PCI.

Diffuse-type ISR was found in 46% of ISR patients and was significantly associated with DM, male sex, LAD and RCA lesions, longer stents, and smaller pre-stenting MLD. These findings are consistent with those of Lee et al.[11] Cassese et al.[10] and Mercado et al.[5] who reported DM and smaller vessel size as predictors of diffuse ISR. However, Park and Park[12] observed no significant association between DM and diffuse ISR (19.6% vs. 28.7%, $P = 0.221$), highlighting discrepancies across datasets. Goldberg et al.[20] further demonstrated that diffuse ISR was associated with smaller reference vessel diameter and longer lesion length; these findings are consistent with our results.

Recent evidence (2020-2024) has further emphasized the evolving epidemiology and management of ISR, highlighting variations across DES generations and in contemporary PCI practices.[2,21,22]

All associations identified in this study should be interpreted cautiously, as they are derived from unadjusted analyses.

Study Limitations

This study has several important limitations that should be considered when interpreting the findings. First, the sample size was modest (n=100; ISR events=50), and no a priori sample size or power calculation was performed; therefore, the study may be underpowered for some comparisons, particularly multivariable modeling, with an increased risk of model overfitting, imprecise effect estimates (wide CIs), and a limited ability to adjust for multiple potential confounders. Second, the focal versus non-focal (diffuse, proliferative, or occlusive) subgroup comparisons were primarily exploratory and largely unadjusted; given the small subgroup counts, comprehensive multivariable adjustment was not feasible, and residual confounding cannot be excluded.

Third, the cohort was restricted to patients undergoing clinically indicated repeat angiography at a single tertiary center, introducing selection and referral biases and limiting generalizability to broader post-PCI populations or to routine surveillance cohorts. Fourth, angiographic assessment relied on QCA when available and on visual estimation otherwise; intravascular imaging (intravascular ultrasound/optical coherence tomography) was not used systematically, which may have led to misclassification of lesion morphology and failure to identify certain mechanisms. Finally, follow-up was short and incomplete for a subset of patients, limiting robust time-to-event analyses and inference regarding longer-term outcomes. Accordingly, the present results should be viewed as hypothesis-generating and warrant confirmation in larger, adequately powered, multicenter studies with standardized imaging and complete longitudinal follow-up. Given the number of ISR events (n=50), inclusion of multiple variables in multivariable modeling may increase the risk of overfitting, and effect estimates should therefore be interpreted with caution.

CONCLUSION

ISR affected half of the patients undergoing clinically indicated repeat angiography and was associated primarily with procedural and angiographic characteristics, including smaller vessel caliber, longer stent length, and LAD involvement. Diffuse ISR showed a trend toward more adverse angiographic characteristics; however, outcome differences were not statistically significant. These findings highlight the need for careful procedural planning and closer follow-up in patients with high-risk angiographic features.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Institutional Review Board of Faculty of Medicine Cairo University (approval no: CMDRF132701/2018, date: 16.01.2018).

Informed Consent: All patients provided written informed consent prior to enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.M.A., F.M.S., Concept: M.A., F.M.S., Design: A.T.E., R.D., Data Collection or Processing: M.A., R.D., Analysis or Interpretation: A.M.A., A.T.E., F.M.S. Literature Search: M.A., F.M.S., Writing: A.M.A., R.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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