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ORIGINAL ARTICLE

Drug-Eluting Balloons Versus Stents for Coronary In-Stent Restenosis: Six-Month Clinical and Angiographic Outcomes

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ABSTRACT

Background: In-stent restenosis (ISR) remains an important complication of percutaneous coronary intervention. Drug-eluting balloon (DEB) angioplasty and repeat drug-eluting stent (DES) implantation are established treatment options, but comparative real-world data from Iraq are limited. This study aimed to compare baseline characteristics and six-month clinical and angiographic outcomes of patients with coronary ISR treated with DEB versus repeat DES implantation.

Methods: This prospective observational study included 200 adults with angiographically confirmed ISR treated in Kirkuk, Iraq, between November 2023 and November 2024. One hundred patients underwent DEB angioplasty and 100 underwent repeat DES implantation in routine practice. Clinical outcome data at six months were available for all patients, and follow-up angiography was performed in 78 DEB-treated and 79 DES-treated patients. The primary clinical outcome was major adverse cardiac events (MACE), defined as the composite of target vessel revascularization, myocardial infarction, and all-cause death.

Results: DES-treated patients had a longer median time to restenosis and a higher prevalence of insulin-dependent diabetes mellitus and family history of coronary artery disease, whereas hypertension was more common in the DEB group. At six months, minimal lumen diameter, late lumen loss, binary restenosis, and target lesion revascularization were comparable between groups. However, TVR and MACE were significantly higher in the DES group. Myocardial infarctions were infrequent and similar in both groups.

Conclusion: DEB and repeat DES showed comparable six-month angiographic outcomes and target lesion revascularization rates. Higher TVR and MACE rates in the DES group may reflect baseline risk differences rather than a device-specific effect.

Key words: In-stent restenosis; Drug-eluting balloon; Drug-eluting stent; Percutaneous coronary intervention; Target vessel revascularization.

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INTRODUCTION

Coronary in-stent restenosis (ISR) represents one of the most persistent challenges in interventional cardiology, occurring in approximately 5–15% of patients following bare-metal stent (BMS) implantation and in 5–10% following drug-eluting stent (DES) implantation in contemporary practice, with rates varying substantially according to patient risk profile, lesion complexity, stent generation, and implantation technique [1, 2]. Although the introduction of second-generation DES substantially reduced ISR rates compared with BMS, ISR continues to account for a clinically significant burden of repeat revascularization procedures and carries non-negligible risks of recurrent target lesion failure and adverse cardiac events [3].

The pathophysiology of ISR is heterogeneous and context dependent. In BMS-ISR, the dominant mechanism is smooth-muscle-cell-mediated neointimal hyperplasia, whereas DES-ISR is more commonly driven by neoatherosclerosis, stent underexpansion, mechanical stent fracture, and polymer hypersensitivity [4]. This mechanistic heterogeneity has direct implications for treatment selection, as distinct pathological substrates respond differently to antiproliferative drug delivery versus mechanical re-expansion. Contemporary guidelines therefore recommend a mechanism-based approach to ISR management, ideally guided by intracoronary imaging [5].

Among available percutaneous treatment strategies, repeat DES implantation and DEB angioplasty have emerged as the most widely adopted guideline-supported options. DEB angioplasty provides localized drug delivery without leaving an additional metallic scaffold—the "leave nothing behind" approach—whereas repeat DES implantation delivers durable antiproliferative scaffolding with potentially greater acute luminal gain [6]. Multiple randomized controlled trials, including the ISAR-DESIRE and RIBS trial series, have demonstrated broadly comparable efficacy between DEB and DES for ISR [7]. The AGENT IDE randomized trial further strengthened the evidence base for drug-coated balloons in coronary ISR by showing that a paclitaxel-coated balloon was superior to an uncoated balloon in reducing target lesion failure [8]. Recent systematic reviews and meta-analyses have corroborated broadly equivalent clinical outcomes between DEB and DES for ISR across most endpoints [9, 10].

Despite this evidence base, treatment selection between DEB and DES in routine practice remains non-protocolized at most centers. Operator judgment, institutional preference, lesion morphology, prior stent type, ISR mechanism, and patient comorbidities collectively shape treatment decisions, introducing systematic differences in the baseline characteristics of patients allocated to each strategy [3, 5]. These real-world selection patterns may significantly confound comparative outcome analyses in observational series, a point that is frequently under-reported in the literature.

An important gap in the existing literature is the paucity of observational data from the Middle East and North Africa (MENA) region, where cardiovascular disease burden, patient comorbidity profiles, and interventional practice patterns may differ from those reported in large Western ISR trials [11, 12]. In Iraq, published interventional cardiology data from single-center practice remain limited, further highlighting the need for local observational studies [13].

Against this background, the present study aimed to: (i) compare the baseline clinical, angiographic, and procedural characteristics of patients with ISR treated with DEB versus DES in routine clinical practice at a tertiary cardiac center in Kirkuk, Iraq; and (ii) compare their six-month clinical and angiographic outcomes, interpreted in the context of the observed baseline differences.

PATIENTS AND METHODS

Study design and setting

This was a prospective, single-center observational comparative study conducted at Azadi Cardiac Centre, Kirkuk, Iraq, a tertiary cardiac facility providing diagnostic and interventional cardiology services to a large catchment population in northern Iraq. The study period spanned 12 consecutive months, from November 2023 to November 2024.

Study population

Eligible participants were adult patients ($\geq$ 18 years) with angiographically confirmed ISR in a previously implanted metallic coronary stent (BMS or DES), treated at Azadi Cardiac Centre during the study period. ISR was defined as a diameter stenosis exceeding 50% within the stent body or within 5 mm of either stent edge on visual coronary angiography. Patients were categorized according to the treatment strategy selected during routine clinical care: DEB angioplasty (n = 100) or repeat DES implantation (n = 100). Treatment allocation was based on the treating interventional cardiologist's clinical judgment.

The choice of treatment with DEB or DES was made by the treating interventional cardiologist according to clinical judgment, lesion characteristics, angiographic findings, and device availability. All eligible patients treated during the study period were enrolled consecutively.

Exclusion criteria were: (i) age < 18 years; (ii) ST-segment elevation myocardial infarction as the index presentation; and (iii) ISR involving a bioresorbable vascular scaffold.

Baseline data collection

The following variables were prospectively recorded: age, sex, time to restenosis (years from index stent implantation to the ISR procedure), previous myocardial infarction, previous CABG, chronic renal failure, diabetes mellitus, insulin-dependent diabetes mellitus, hypertension, hypercholesterolemia, family history of coronary artery disease, current smoking, clinical presentation (stable angina vs. acute coronary syndrome [ACS]), target vessel, index stent family, DES subtype (when applicable), ISR morphological classification (Mehran classification: focal, diffuse intrastent, proliferative, or occlusive) [14], and pre-dilation status. The unit of analysis was the individual patient.

Follow-up protocol and outcome definitions

All patients underwent clinical follow-up at six months after the index ISR procedure. Follow-up was conducted via outpatient clinic attendance or, when applicable, structured telephone contact. Clinical status at follow-up was categorized as stable, recurrent angina, or ACS.

Follow-up angiography was performed at approximately six months in patients with recurrent angina, acute coronary syndrome, objective evidence of ischemia, or when requested by the treating cardiologist according to institutional practice. It was not routinely mandated for all patients because this was a real-world observational study rather than a protocol-driven trial.

The following outcomes were assessed at six-month follow-up:

- Angiographic outcomes among patients who underwent repeat coronary angiography: minimal lumen diameter (MLD, mm), late lumen loss (LLL, mm; defined as MLD immediately after the procedure minus MLD at follow-up), and binary restenosis (diameter stenosis $\geq$ 50% at follow-up angiography).
- Clinical outcomes in the intent-to-treat population (n = 200): (i) target lesion revascularization (TLR), defined as any repeat revascularization of the original target lesion; (ii) target vessel revascularization (TVR), defined as any repeat revascularization of any segment of the target vessel, including the target lesion; (iii) non-TLR TVR, defined as TVR events not attributable to the original target lesion; (iv) myocardial infarction (MI); (v) all-cause death; (vi) cardiovascular death; and (vii) major adverse cardiac events (MACE), defined as a pre-specified composite of TVR, MI, and all-cause death.

Late lumen loss was calculated as the difference between post-procedural minimal lumen diameter and minimal lumen diameter at six-month follow-up angiography.

Statistical analysis

Statistical analysis was performed using Python version 3.11 with the SciPy library. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed continuous variables are presented as mean $\pm$ standard deviation (SD) and compared using the independent-samples t-test. Non-normally distributed continuous variables are presented as median and interquartile range (IQR) and compared using the Mann–Whitney U test. Categorical variables are presented as frequencies and percentages and compared using Pearson's chi-square test or Fisher's exact test, as appropriate. A two-sided P-value of < 0.05 was considered statistically significant. No correction for multiple comparisons was applied; all comparisons should be interpreted descriptively and exploratorily given the observational design. No adjusted or sensitivity analysis was performed; therefore, all outcome comparisons should be interpreted as unadjusted exploratory findings.

No formal a priori sample size calculation was performed. The enrollment target of 200 patients, with 100 patients in each treatment group, was determined pragmatically based on the expected number of eligible ISR cases during the 12-month study period, feasibility of follow-up, and the aim of obtaining balanced DEB and DES comparison groups in this exploratory observational study.

RESULTS

Baseline clinical characteristics

A total of 200 patients with angiographically confirmed ISR were included: 100 treated with DEB angioplasty and 100 with repeat DES implantation. Baseline characteristics are presented in Table 1. The mean age was 60.0 $\pm$ 12.0 years in the DEB group and 63.0 $\pm$ 11.0 years in the DES group (P = 0.067). Male sex was present in 65% of DEB-treated and 75% of DES-treated patients (P = 0.165). Median time to restenosis was significantly shorter in the DEB group (2.90 [IQR 1.85–4.04] vs. 4.30 [IQR 3.45–5.68] years; $P < 0.001$).

The prevalence of previous myocardial infarction (72% vs. 73%), previous CABG (19% vs. 22%), chronic renal failure (9% vs. 10%), overall diabetes mellitus (54% vs. 44%), hypercholesterolemia (63% vs. 71%), and current smoking (45% vs. 44%) did not differ significantly between groups (all $P > 0.05$). However, insulin-dependent diabetes mellitus was significantly more prevalent in the DES group (33% vs. 16%; P = 0.009), hypertension was significantly more prevalent in the DEB group (76% vs. 55%; P = 0.003), and family history of coronary artery disease was significantly more common in the DES group (65% vs. 34%; $P < 0.001$). Clinical presentation was similar between groups (P = 0.256).

Table 1. Baseline clinical characteristics of the studied groups.

Characteristic	DEB (n = 100)	DES (n = 100)	*P*-value
Demographics			
Age (years)	60.0 ± 12.0	63.0 ± 11.0	0.067
Male sex	65 (65%)	75 (75%)	0.165
Time to restenosis (years)	2.90 (1.85–4.04)	4.30 (3.45–5.68)	< **0.001**
Medical history			
Previous myocardial infarction	72 (72%)	73 (73%)	0.999
Previous CABG	19 (19%)	22 (22%)	0.726
Chronic renal failure	9 (9%)	10 (10%)	0.999
Cardiovascular risk factors			
Diabetes mellitus	54 (54%)	44 (44%)	0.203
Insulin-dependent DM	16 (16%)	33 (33%)	**0.009**
Hypertension	76 (76%)	55 (55%)	**0.003**
Hypercholesterolemia	63 (63%)	71 (71%)	0.292
Family history of CAD	34 (34%)	65 (65%)	< **0.001**
Current smoker	45 (45%)	44 (44%)	0.999
Clinical presentation			
Stable angina	59 (59%)	50 (50%)	0.256
Acute coronary syndrome	41 (41%)	50 (50%)	0.256

DEB, drug-eluting balloon; DES, drug-eluting stent; CABG, coronary artery bypass grafting; DM, diabetes mellitus; CAD, coronary artery disease. Values are mean ± SD, median (IQR), or n (%).

Angiographic and procedural characteristics at index procedure

Angiographic and procedural characteristics are presented in Table 2. Target vessel distribution was comparable between groups (P = 0.937). The right coronary artery was the most frequently treated vessel in the DEB group (42%), whereas the LAD and RCA were equally prevalent in the DES group (37% and 38%). The index stent family did not differ significantly (P = 0.553), with BMS being the most common index stent in both groups (66% DEB, 67% DES). ISR morphological classification was similar between groups (P = 0.841), with focal ISR being the most prevalent pattern (48% DEB, 53% DES). Pre-dilation was performed in all DEB-treated patients (100%) versus 86% of DES-treated patients (P < 0.001).

Six-month follow-up: completeness and clinical status

Six-month clinical outcome data were available for all patients in both groups. At follow-up, 79% of DEB-treated and 81% of DES-treated patients were clinically stable, 18% and 16% had recurrent angina, and 3% in each group presented with acute coronary syndrome. Repeat coronary angiography at approximately six months was available in 78 DEB-treated and 79 DES-treated patients. Full follow-up and outcome data are presented in Table 3.

Six-month angiographic outcomes

Repeat coronary angiography at approximately six months was performed in 78 DEB-treated and 79 DES-treated patients. Mean MLD at follow-up was 2.12 ± 0.45 mm in the DEB group and 2.15 ± 0.42 mm in the DES group (P = 0.715). Median LLL was 0.38 (IQR 0.20–0.55) mm in the DEB group and 0.39 (IQR 0.14–0.61) mm in the DES group (P = 0.798). Binary restenosis occurred in 8 of 78 DEB-treated patients (10.3%) and in 12 of 79 DES-treated patients (15.2%); this difference was not statistically significant (P = 0.474).

Six-month clinical outcomes

In the intent-to-treat population (n = 200), TLR rates were similar between groups (8.0% DEB vs. 9.0% DES; P = 0.999). TVR occurred in 13 DEB-treated patients (13.0%) and 25 DES-treated patients (25.0%), representing a statistically significant difference (P = 0.047). The excess TVR in the DES group was driven predominantly by non-TLR TVR events (16% DES vs. 5% DEB), whereas TLR-associated TVR was comparable. MI occurred in 3% of each group (P = 0.999), all-cause death in 2% DEB versus 1% DES (P = 0.999), and cardiovascular death in 1% of each group (P = 0.999).

MACE, the composite of TVR, MI, and all-cause death, occurred in 16 DEB-treated patients (16.0%) and 29 DES-treated patients (29.0%), a statistically significant difference (P = 0.042). The higher MACE rate in the DES group was attributable primarily to the excess TVR events rather than to differences in MI or mortality.

Table 2. Angiographic and procedural characteristics of the studied groups.

Characteristic	DEB (n = 100)	DES (n = 100)	*P*-value
Target vessel			
Left anterior descending artery	31 (31%)	37 (37%)	0.937
Circumflex artery	25 (25%)	23 (23%)	
Right coronary artery	42 (42%)	38 (38%)	
Left main coronary artery	1 (1%)	1 (1%)	
Saphenous vein graft	1 (1%)	1 (1%)	
Index stent family			
Bare-metal stent	66 (66%)	67 (67%)	0.553
Drug-eluting stent	24 (24%)	27 (27%)	
Unknown	10 (10%)	6 (6%)	
ISR morphological classification (Mehran)			
Focal	48 (48%)	53 (53%)	0.841
Diffuse intrastent	36 (36%)	34 (34%)	
Proliferative	10 (10%)	7 (7%)	
Occlusive	6 (6%)	6 (6%)	
Procedural			
Pre-dilation performed	100 (100%)	86 (86%)	**< 0.001**

LAD, left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; LM, left main; SVG, saphenous vein graft; BMS, bare-metal stent; ISR, in-stent restenosis.
Values are n (%). For multi-category variables, the *P*-value is shown for the overall group comparison in the first row.

Table 3. Six-month follow-up and clinical outcomes.

Outcome	DEB (n = 100)	DES (n = 100)	*P*-value
Clinical status at follow-up			
Clinically stable	79 (79%)	81 (81%)	0.855
Recurrent angina	18 (18%)	16 (16%)	0.849
Acute coronary syndrome	3 (3%)	3 (3%)	0.999
Angiographic outcomes (patients with six-month angiography: DEB n = 78, DES n = 79)			
Minimal lumen diameter (mm)	2.12 ± 0.45	2.15 ± 0.42	0.715
Post-procedural MLD (mm)	2.51 ± 0.53	2.55 ± 0.51	0.610
Late lumen loss (mm)	0.38 (0.20–0.55)	0.39 (0.14–0.61)	0.798
Binary restenosis	8/78 (10.3%)	12/79 (15.2%)	0.474
Clinical outcomes at six-month follow-up (intent-to-treat, n = 200)			
Target lesion revascularization (TLR)	8 (8.0%)	9 (9.0%)	0.999
Target vessel revascularization (TVR)	13 (13.0%)	25 (25.0%)	**0.047**
Non-TLR TVR	5 (5.0%)	16 (16.0%)	**0.011**
Myocardial infarction	3 (3.0%)	3 (3.0%)	0.999
All-cause death	2 (2.0%)	1 (1.0%)	0.999
Cardiovascular death	1 (1.0%)	1 (1.0%)	0.999
MACE (composite)[†]	16 (16.0%)	29 (29.0%)	**0.042**

MLD, minimal lumen diameter; LLL, late lumen loss; TLR, target lesion revascularization; TVR, target vessel revascularization; MI, myocardial infarction; MACE, major adverse cardiac events.
MLD values are mean ± SD; LLL values are median (IQR); all other values are n (%).
P-values for clinical status categories are row-wise comparisons.
[†] MACE was defined as the composite of TVR, MI, and all-cause death. Angiographic outcomes were assessed only in patients who underwent six-month follow-up angiography. Clinical outcomes were assessed in the intent-to-treat population (n = 200).

DISCUSSION

This single-center observational study compared the baseline characteristics and six-month clinical and angiographic outcomes of 200 patients with coronary ISR treated with DEB angioplasty or repeat DES implantation in routine clinical practice. The main findings were: (i) angiographic outcomes—MLD, LLL, and binary restenosis—were similar between groups at six months; (ii) TLR rates were comparable (8% vs. 9%); (iii) TVR was significantly higher in the DES group (25% vs. 13%; $P = 0.047$), driven primarily by non-TLR TVR events; (iv) MACE occurred in significantly more DES-treated patients (29% vs. 16%; $P = 0.042$); and (v) MI and death were low and comparable. Importantly, the DES group had a higher-risk baseline profile, including greater prevalence of insulin-dependent diabetes and family history of coronary artery disease, which likely contributed substantially to the

observed outcome differences.

The absence of significant differences in MLD (2.12 vs. 2.15 mm; P = 0.715), LLL (0.38 vs. 0.39 mm; P = 0.798), and binary restenosis (10.3% vs. 15.2%; P = 0.474) between DEB and DES groups is consistent with the majority of published evidence. The landmark AGENT IDE randomized trial demonstrated that a paclitaxel-coated balloon was superior to an uncoated balloon for coronary ISR, further supporting the role of drug-coated balloons as an effective treatment strategy in this setting [8]. Similarly, the RIBS V and ISAR-DESIRE 3 trials reported comparable angiographic outcomes between DEB and DES for DES-ISR [15, 16]. A recent meta-analysis by Kumar et al. [9] and a trial sequential analysis by Abdelaziz et al. [10], encompassing multiple randomized trials, confirmed no significant difference in binary restenosis or LLL between DEB and DES for ISR across various stent subtypes. The present observational data align well with this body of evidence, supporting the real-world applicability of the DEB-versus-DES equivalence observed in randomized trials.

The binary restenosis rates observed in the present cohort—10.3% for DEB and 15.2% for DES—are within the range reported in contemporary ISR registries, which typically report rates of 10–20% at six to nine months depending on lesion complexity and patient risk profile [17, 18]. The numerically higher rate in the DES group (P = 0.474) is consistent with the higher-risk baseline phenotype of these patients rather than with device inferiority.

TLR, the most lesion-specific measure of treatment success, was equivalent between groups (8.0% vs. 9.0%; P = 0.999). This finding directly supports the clinical equivalence of DEB and DES in controlling neointimal recurrence at the treated ISR lesion under real-world conditions and is consistent with TLR rates of 8–14% reported in contemporary ISR trials comparing these two strategies [19]. The TLR data from this observational cohort thus corroborate randomized trial findings despite the non-randomized design and the significant baseline differences between groups.

The significantly higher TVR rate in the DES group (25% vs. 13%; P = 0.047) and the resulting excess MACE (29% vs. 16%; P = 0.042) are important findings that require careful contextual interpretation. These findings should be interpreted in light of the baseline differences between groups. The DES group had a higher prevalence of insulin-dependent diabetes mellitus, a stronger family history of coronary artery disease, and a longer time to restenosis, all of which may indicate a higher underlying atherosclerotic risk profile. Therefore, the higher TVR and MACE rates observed in the DES group are more likely to reflect baseline clinical selection and greater disease burden than a true device-specific disadvantage of repeat DES implantation. This distinction is important when interpreting comparative outcomes in non-randomized real-world studies.

Crucially, the TVR excess was driven almost entirely by non-TLR TVR events (16% DES vs. 5% DEB), meaning that the additional revascularization procedures in DES-treated patients were performed predominantly for disease in segments of the target vessel other than the original ISR lesion. This finding is highly consistent with the significantly higher-risk cardiovascular baseline profile of DES-treated patients in this cohort: greater insulin-dependent diabetes prevalence (33% vs. 16%), higher family history of coronary artery disease (65% vs. 34%), and longer time to restenosis—a combination associated with more diffuse and progressive coronary atherosclerosis [9, 10].

Insulin-treated diabetes is a well-established independent predictor of diffuse coronary disease, accelerated atherosclerosis, and higher rates of recurrent revascularization across all treatment modalities [20]. The strong familial coronary disease burden in the DES group further reinforces the notion of a more aggressive atherosclerotic phenotype in these patients. In this context, the higher non-TLR TVR rate in the DES group most plausibly reflects progressive disease at non-target lesion sites within the target vessel, a process related to patient biology rather than to the device used to treat the index ISR lesion. Clinically, these findings suggest that higher TVR and MACE rates in observational DES-treated cohorts may reflect patient selection and more advanced vessel disease rather than reduced lesion-level efficacy of repeat DES implantation.

This interpretation is consistent with observations from contemporary ISR trials and registries. In the RIBS V trial, DES-treated patients had numerically higher TVR rates despite comparable TLR, a pattern attributed in part to disease progression at non-target sites [21]. Likewise, the meta-analysis by Kumar et al. [9] noted that although TLR and binary restenosis were comparable between DEB and DES, TVR and MACE showed numerically higher rates in observational subgroups with greater comorbidity burden. The present data add further observational evidence from a distinct geographic and clinical context.

Given that this study was non-randomized and that treatment allocation was systematically associated with the very baseline factors that predict TVR and MACE (insulin-dependent diabetes and family history of CAD), attributing the TVR and MACE differences to device-specific effects would be methodologically inappropriate. The observed outcome differences should therefore be interpreted as a consequence of non-random treatment selection rather than as evidence of clinical inferiority of DES over DEB.

MI (3% in each group; P = 0.999), all-cause death (2% vs. 1%; P = 0.999), and cardiovascular death (1% vs. 1%; P = 0.999) were low and comparable between groups. These findings are consistent with the well-established safety profile of both

DEB and DES for ISR treatment in contemporary practice and are concordant with the pooled safety data from recent meta-analyses [9, 10]. The low event rates in both groups are also consistent with a population treated at a single experienced center, where procedural care standards are consistent.

This study provides prospective follow-up data from a real-world ISR cohort in northern Iraq, a context that is substantially underrepresented in the ISR literature [2, 3]. The predominance of BMS as the index stent (approximately 66–67%), the high metabolic comorbidity burden, and the clinical practice patterns at this center reflect important regional characteristics that are not captured in European or North American trial populations [22]. Despite these contextual differences, the angiographic outcomes and TLR rates observed in the present cohort are remarkably consistent with those from landmark trials, suggesting that the device-level efficacy of DEB and DES for ISR is generalizable across diverse clinical settings [10, 23]. This is an important and novel observation for the regional literature.

From a practical standpoint, these findings suggest that outcome differences between DEB and DES in observational cohorts should be interpreted cautiously unless baseline risk imbalance is adequately accounted for.

This study has several limitations that should be considered when interpreting the findings. It was a single-center observational study without random treatment allocation; therefore, baseline differences between the DEB and DES groups, particularly insulin-dependent diabetes, family history of CAD, and time to restenosis, may have influenced the observed differences in TVR and MACE. Although consecutive eligible patients were included, no formal sample size calculation or propensity-score adjustment was performed, and residual confounding cannot be excluded. In addition, six-month angiography was not mandatory for all patients and was performed according to clinical indication or institutional practice, which may have introduced selection bias because patients undergoing repeat angiography were more likely to have recurrent symptoms or suspected ischemia. Intracoronary imaging was not routinely used, limiting detailed assessment of ISR mechanisms. Some pharmacological and procedural variables, such as antiplatelet therapy, statin use, balloon sizing, inflation pressure, and adjunctive lesion preparation, were also unavailable.

Future studies should use multicenter prospective designs with predefined treatment-selection criteria, larger sample sizes, and appropriate risk adjustment or propensity matching. Routine intracoronary imaging, standardized angiographic follow-up, complete pharmacological and procedural data collection, and longer follow-up periods would provide stronger evidence regarding the comparative effectiveness of DEB and DES for coronary ISR, particularly in real-world populations from the MENA region.

CONCLUSION

In this single-center prospective observational study of 200 patients with coronary ISR treated in routine clinical practice, DEB angioplasty and repeat DES implantation demonstrated comparable angiographic outcomes at six months, including MLD, LLL, and binary restenosis, as well as equivalent TLR rates. MACE and TVR were significantly higher in the DES group, a difference attributable primarily to non-TLR TVR events and likely reflecting the higher-risk cardiovascular profile of patients selected for DES rather than a device-specific effect. These findings should therefore be interpreted cautiously in light of the baseline risk imbalance between groups. MI and death were low and similar between groups. These findings support the clinical applicability of DEB as an effective percutaneous strategy for ISR in real-world practice, consistent with evidence from randomized trials, while highlighting the important impact of non-random treatment selection on observational outcome comparisons. Prospective, adequately powered studies with pre-specified allocation criteria, routine intracoronary imaging, and complete follow-up are needed to generate definitive comparative evidence in this setting.

ETHICAL DECLARATIONS

- **Ethics Approval and Consent to Participate**

  The study protocol was approved by the Research Ethics Committee of the College of Medicine, University of Kirkuk, Iraq (Approval No. 55B; dated 30 October 2023). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment.

- **Consent for Publication**

  Not applicable.

- **Availability of Data and Material**

  The data supporting the findings of this study are available from the corresponding author upon reasonable request.

- **Competing Interests**

  The authors declare that they have no conflicts of interest.

- **Funding**

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- **Use of Generative Artificial Intelligence**

The authors declare that ChatGPT (OpenAI) was used solely for language editing and improvement of grammar and sentence clarity during manuscript preparation. It was not used for data generation, statistical analysis, interpretation of results, or clinical decision-making. All AI-assisted outputs were carefully reviewed by the authors, who take full responsibility for the accuracy, integrity, and final content of the manuscript.

- **Authors' Contributions**

RHN conceived the study, supervised data collection, and contributed to drafting the manuscript. MAN contributed to study design, data analysis, literature review, and manuscript revision. IAY contributed to data verification, follow-up case review, interpretation of findings, and critical revision of the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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