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Original research

RESEARCH ON RESTENOSIS CHARACTERISTICS AND RELATED FACTORS IN PATIENTS AFTER CORONARY ARTERY INTERVENTION WITH DRUG - ELUTING STENTS

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ABSTRACT

Objectives: *To evaluate the characteristics of in-stent restenosis (ISR) and its associated risk factors in patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DES), and to assess their clinical implications.*

Methods: *This cross-sectional descriptive study included 70 patients who had undergone PCI with DES and were diagnosed with ISR within two years post-intervention at the Cardiovascular Center, Hue Central Hospital, from March 2021 to August 2023. Data were collected on demographic characteristics, cardiovascular risk factors, lesion properties, and restenosis severity. Multivariate logistic regression was performed to identify independent risk factors for ISR.*

Results: *The 70 patients in the study had an average age of 70.43 ± 8.99 years, 67.14% were male. Restenosis of the anterior interventricular artery accounted for the highest rate of about 61.4%. The rate of strict restenosis (≥70%) accounted for 67.1% in the 2 groups. The average length of stenosis was 16.73 ± 10.48 mm. The length of the lesion in the DES 1 group (14.04 ± 5.78 mm) was shorter than that in the DES 2 group (20.77 ± 14.22 mm) with $p < 0.05$ and the DES 2 group had a more localized stenosis than the DES 1 group with $p < 0.05$. Key risk factors for ISR included diabetes, renal failure, and dyslipidemia. Additionally, post-interventional vessel diameter, lesion length, and the use of first-generation DES were significantly associated with diffuse ISR ($p < 0.05$).*

Conclusion: *ISR remains a major challenge in PCI with DES. It is influenced by lesion characteristics, patient comorbidities, and stent generation. Further prospective studies are required to confirm these findings and develop targeted prevention strategies.*

Keywords: *Coronary artery disease, in-stent restenosis, drug-eluting stents, percutaneous coronary intervention, risk factors.*

I. INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of mortality and disability-adjusted life years (DALYs) globally, responsible for approximately 7 million deaths and 129 million DALYs annually [1-3]. According to the latest cardiovascular and stroke statistics from the American Heart Association, about 660,000 Americans are newly diagnosed with CAD each year, with an incidence rate indicating that one American suffers a myocardial infarction (MI) every 34 seconds, and one person dies from CAD every 1 minute and 24 seconds [4]. Data reported by Pham Viet Tuan and Nguyen Lan Viet indicate a significant increase in the prevalence of ischemic heart disease treated at the National Heart Institute of Vietnam, from 11.3% in 2003 to 24% in 2007 among total admissions [5].

Percutaneous coronary intervention (PCI) with drug-eluting stents (DES) has significantly improved outcomes for patients with coronary artery disease (CAD). However, in-stent restenosis (ISR) remains a major clinical challenge, affecting 3% to 20% of patients depending on patient-specific and procedural factors [1, 2]. ISR is a complex phenomenon influenced by multiple mechanisms,

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including neointimal hyperplasia, inflammation, and delayed vascular healing [3, 4].

While numerous studies have examined ISR risk factors, there remains a lack of region-specific data on ISR characteristics and outcomes in the Vietnamese population. This study adds new insights by evaluating ISR patterns in a real-world cohort of PCI patients in Vietnam, where cardiovascular risk profiles and treatment practices may differ from Western populations. Additionally, while previous research has established associations between ISR and comorbidities such as diabetes and dyslipidemia, this study provides a more detailed analysis of ISR severity and lesion-specific predictors using multivariate regression. The study also explores the differential impact of first- and second-generation DES on restenosis patterns, contributing to the ongoing discussion on optimal stent selection. These findings may help refine patient-specific ISR risk assessment and guide improvements in interventional cardiology practices [10, 11].

Despite extensive research, there is limited data on ISR risk factors in the Vietnamese population. Understanding patient-specific and lesion-specific determinants of ISR in this population is essential for optimizing PCI outcomes. Therefore, this study was conducted with two primary objectives: (1) to investigate the characteristics of ISR two years after PCI with DES and (2) to evaluate the clinical and lesion-related risk factors associated with ISR in a Vietnamese cohort. By identifying key predictors, this study aims to contribute to risk stratification and the development of targeted ISR prevention strategies.

II. MATERIALS AND METHODS

2.1. Study population

The study included 70 patients who underwent successful percutaneous coronary intervention (PCI) with drug-eluting stents (DES) over a two-year period at the Emergency and Interventional Cardiology Department, Cardiovascular Center, Hue Central Hospital, from March 2021 to August 2023.

Inclusion criteria were patients were diagnosed with in-stent restenosis (ISR), confirmed by coronary angiography showing ≥ 50% restenosis at the stent site or within 5 mm of the stent edges; Patients had a history of PCI with DES within the last two years.

Exclusion criteria were coronary angiography showed < 50% stenosis at the stent site or stenosis outside the stent location; Patients who were unable to undergo coronary angiography.

2.2. Study methods

Data collection and patient selection:

Seventy patients who had undergone PCI with DES within the past two years and were diagnosed with ISR were included in the study. ISR was confirmed through coronary angiography, defined as ≥ 50% luminal narrowing at the stented segment or within 5 mm of the stent edge.

Demographic data, medical history, clinical parameters, and laboratory findings were collected. Risk factors such as diabetes, hypertension, dyslipidemia, chronic kidney disease, and smoking status were recorded. Procedural factors, including lesion location, stent generation, and post-intervention vessel diameter, were assessed. ISR was further categorized into focal (≤ 10 mm in length) and diffuse (> 10 mm in length) restenosis.

Assessment of restenosis severity:

ISR severity was classified into moderate (50% to < 70% stenosis) and severe (≥ 70% stenosis) based on quantitative coronary angiography (QCA). The minimum lumen diameter and percentage of diameter stenosis were measured using MedCalc software, ensuring objective and reproducible assessment.

Statistical analysis:

All statistical analyses were performed using SPSS 20.0 and MedCalc software. Descriptive statistics were used to summarize continuous variables as mean ± standard deviation (SD) and categorical variables as frequencies and percentages.

To identify risk factors associated with in-stent restenosis (ISR), we conducted univariate logistic regression analysis, followed by multivariate logistic regression to determine independent predictors of ISR. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported, and a p-value < 0.05 was considered statistically significant. Additionally, correlation analyses were performed to examine relationships between lesion characteristics and restenosis severity.

III. RESULTS

3.1. Characteristics of the study population

Among the 70 patients included in the study, the majority were male, comprising 67.14% of the population, with a mean age of 70.43 ± 8.99 years. Risk factors for coronary artery disease, such as smoking, hypertension, and diabetes, were prevalent within the study group (Table 1). Among the 70 patients, the majority (91.4%) had restenosis involving only one coronary artery branch (Table 2).

Table 1: General characteristics of the study population

Characteristic		Number of Patients (n)	Percentage (%)
Mean Age (years)		70.43 ± 8.99 (years)	
Sex	Male	47	67.14
	Female	23	32.86
Smoking		55.7	
Hypertension		94.3	
Diabetes		48.6	
Kidney failure		40	
Heart rate		80.67 ± 14.88 bpm	
Systolic blood pressure		136.7 ± 27.75 mmHg	
Diastolic blood pressure		79.14 ± 11.76 mmHg	

Table 2: Characteristics of restenosis branches number

Number of Restenosis Branches	Total (n=70)	Percentage (%)
1 branch	63	90
2 branches	6	8.6
3 branches	1	1.4

In the study cohort, 60% of patients were treated with first-generation drug-eluting stents, while 40% received second-generation stents (Table 3). The mean stent length was 16.66 ± 10.54 mm, with a mean reference vessel diameter of 2.90 ± 0.58 mm. The mean vessel diameter before intervention was 0.78 ± 0.18 mm, and after intervention, it was 2.78 ± 0.35 mm (Table 4).

Table 3: Generations of drug-eluting stents

Stent Generation	Number	Percentage (%)
First generation	42	60.0
Second generation	28	40.0

Table 4: Stent characteristics

	$\bar{X}$ ± SD	Min	Max
Restenosis stent length (mm)	16.73 ± 10.48	6.26	45
Reference vessel diameter (mm)	2.90 ± 0.58	2	4,21
Diameter before intervention (mm)	0.78 ± 0.18	0.04	1.1
Diameter after intervention (mm)	2.77 ± 0.35	2.17	3.75

3.2. Patient factors related to in-stent restenosis after coronary intervention with drug-eluting stents

Patients with dyslipidemia had a higher incidence of diffuse restenosis compared to focal restenosis, with rates of 77.5% and 50%, respectively. This difference was statistically significant ($p < 0.05$) (Table 5). Dyslipidemia was associated with a higher risk of diffuse restenosis compared to focal restenosis, with an OR of 3.44 (95% CI: 1.23-9.66, $p < 0.05$), having statistical significance (Table 6).

Table 5: Patient factors associated with restenosis patterns

Patient Factors		Focal restenosis (n = 30)	Diffuse restenosis (n = 40)	p
Diabetes Mellitus	n	14	20	> 0.05
	%	46.7%	50%	
Hypertension	n	29	37	> 0.05
	%	96.7%	92.5%	
Kidney Failure	n	11	17	> 0.05
	%	36.7%	42.5%	
Dyslipidemia	n	15	31	< 0.05
	%	50%	77.5%	
Smoking	n	15	24	> 0.05
	%	38.5%	61.5%	
Female Sex	n	9	14	> 0.05
	%	30%	35%	

Table 6: Univariate analysis of patient factors associated with restenosis patterns

Patients factor	OR	Confidence interval 95%	p
Age	0.97	0.92 - 1.03	> 0.05
Male Sex	1.26	0.46 - 3.47	> 0.05
Diabetes	1.14	0.44 - 2.95	> 0.05
Kidney Failure	1.28	0.48 - 3.37	> 0.05
Dyslipidemia	3.44	1.23 - 9.66	< 0.05
Smoking	1.5	0.58 - 3.90	> 0.05
Hypertension	0.425	0.04 - 4.31	> 0.05

3.3. Stent-related factors associated with restenosis patterns

Among the 70 patients studied, there was no significant difference in the location of restenosis between focal and diffuse patterns (Table 7). Focal restenosis was more common in patients with second-generation DES than with first-generation DES. The second-generation DES was associated with a higher rate of focal restenosis, with an OR of 0.29 (95% CI: 0.107-0.790, $p < 0.05$) (Table 8).

Table 7: Comparison of lesion location and restenosis patterns

Lesion Location		Focal restenosis (n = 30)	Diffuse restenosis (n = 40)	p
Left Anterior Descending Artery	n	20	30	> 0.05
	%	66.7%	75%	
Right Coronary Artery	n	9	12	> 0.05
	%	30%	30%	
Circumflex Artery	n	3	4	> 0.05
	%	10%	10%	

Table 8: Comparison of drug-eluting stent generations and restenosis patterns

DES Generation	Focal restenosis (n = 30)	Diffuse restenosis (n = 40)	OR	95% CI	p
DES 1 (n=42)	31% (n=13)	69% (n=29)	0.29	0.107-0.790	< 0.05
DES 2 (n=28)	60.7% (n=17)	39.3% (n=11)			

Lesion length was greater in the diffuse restenosis group compared to the focal restenosis group, with mean lengths of 24.62 ± 10.89 mm and 18.03 ± 7.87 mm, respectively (OR: 1.08, 95% CI: 1.02 - 1.15, p < 0.05). The mean post-intervention diameter was larger in the focal restenosis group (2.88 ± 0.37 mm) than in the diffuse group (2.69 ± 0.31 mm), with an OR of 0.169 (95% CI: 0.038-0.74, p < 0.05). Other factors, such as reference vessel diameter and pre-intervention diameter, showed no significant differences between groups (Table 9). Diabetes, kidney failure, and hypertension significantly statistically increased the severity of coronary restenosis. Lesion length increase 0.58% in lumen diameter for each millimeter of lesion length with regression coefficient of 0.58 (95% CI: 0.19 - 0.97, p < 0.05) (Table 10). Lesion length was significantly associated with the degree of restenosis, with a regression coefficient of 0.49 (95% CI: 0.09 - 0.88, p < 0.05). Kidney failure also increased the risk of severe in-stent restenosis, with a regression coefficient of 8.31 (95% CI: 0.45 - 16.17, p < 0.05) (Table 11).

Table 9: Comparison of stent characteristics and restenosis patterns

Stent Characteristics	$\bar{X}$ ± SD		OR	95% CI	p
	Focal restenosis (n=30)	Diffuse restenosis (n=40)			
Lesion length (mm)	18.03 ± 7,87	24.62 ± 10.89	1.08	1.02-1,15	< 0.05
Reference Vessel Diameter (mm)	3.01 ± 0.67	2.82 ± 0.49	2.57	0.75-8.77	> 0.05
Pre-Intervention Diameter (mm)	0.82 ± 0.14	0.75 ± 0.21	0.58	0.246-1.323	> 0.05
Post-intervention diameter (mm)	2.88 ± 0.37	2.69 ± 0.31	0.169	0.038-0.74	< 0.05
Stent Duration (months)	12.94 ± 3.93	14.23 ± 3.77	1.088	0.957-1.236	> 0.05

3.4. Stent-related factors influencing the degree of in-stent restenosis

Table 10: Univariate analysis of factors related to the degree of restenosis

Factor	Regression coefficient	95% CI	p
Hypertension	-1.28	-19.23 - 16.67	< 0.05
Diabetes Mellitus	8.78	0.72 - 16.84	< 0.05
Kidney Failure	8.86	0.63 - 17.09	< 0.05
Dyslipidemia	9.83	1.38 - 18.28	< 0.05
Lesion Length	0.58	0.19 - 0.97	< 0.05

Table 11: Multivariate regression analysis of factors associated with the degree of restenosis

Factor	Regression Coefficient	95% Confidence Interval (CI)	p
Diabetes Mellitus	4.05	-3.99-12.1	> 0.05
Kidney Failure	8.31	0.45-16.17	< 0.05
Dyslipidemia	4.83	-3.83-13.49	> 0.05
Lesion Length (mm)	0.49	0.09-0.88	< 0.05

IV. DISCUSSION

The mean age of the study population was 70.43 ± 8.99 years, with the youngest participant being 51 years old and the oldest 90, which is higher than in some domestic studies on in-stent restenosis (ISR), such as that by Nguyen Thi Hai Yen [9], where the mean age was 66.9 ± 8.9 years. Male patients predominated, accounting for 67.14% of the cohort, with a male-to-female ratio of 2:1, similar to the findings of Nguyen Thi Hai Yen [9].

Regarding cardiovascular risk factors, hypertension and dyslipidemia were the most common, with prevalence rates of 94.3% and 65.7%, respectively, followed by diabetes mellitus (48.6%) and obesity (11.4%). The proportion of diabetic patients among patient with in-stent re-stenosis after DES placement in our study (48.6%), which was higher than in other domestic studies, such as those by Nguyen Thi Hai Yen and Kim et al., where diabetes prevalence was reported at 37.5% and 38.1% for early and late ISR, respectively [8], [9]. The prevalence of hypertension was also predominant (94.3%) in this study, exceeding the rates observed in domestic and international research, including studies by Nguyen Thi Hai Yen (2020) [8] and Michael Ragosta et al. (2003) [10]. The proportions of patients with dyslipidemia, smoking, and chronic kidney disease were 65.7%, 55.7%, and 40%, respectively, all of which are cardiovascular risk factors associated with coronary artery atherosclerosis.

The most common lesion location was the left anterior descending artery (LAD), accounting for 61.4%, followed by the right coronary artery (26.9%) and the circumflex artery (12.7%). These findings are consistent with other domestic and international studies that also reported a high prevalence of ISR in the LAD. For instance, in the study by Nguyen Minh Hung, LAD lesions comprised 50%, while in the study by Zheng et al., the proportion was 60.9% [11]. This is reasonable because the left and right coronary arteries are the two main branches supplying the myocardium, and they are frequently affected in clinical cases. The bifurcations of left anterior descending artery and the right coronary artery have many angulated and bifurcated areas, contribute to higher ISR rates at these sites.

We categorized the study subjects into two groups: moderate restenosis (50% to < 70%) and severe restenosis (≥ 70%). The results showed that severe restenosis was more prevalent (67.1%), similar to the findings of Nguyen Thi Hai Yen,

where severe ISR was more common than moderate ISR (53.6%) [8]. In our study, 30 patients (42.86%) had diffuse restenosis, while 40 patients (57.14%) had focal restenosis. The mean lesion length was 16.73 ± 10.48 mm, consistent with international studies such as that by Schofer et al., where the mean lesion length was 14.9 mm [12]. The mean reference vessel diameter was 2.90 ± 0.58 mm, a mean minimum lumen diameter of 0.78 ± 0.18 mm before intervention and 2.77 ± 0.35 mm after intervention, comparable to the findings of Ragosta et al. [15].

There was no significant differences in clinical characteristics, such as diabetes, kidney failure, hypertension, dyslipidemia, and smoking, were observed between the two generations of drug-eluting stents (DES). This is in line with the findings of Kilickesmez et al., who reported no significant differences in the prevalence of diabetes, smoking, and hypertension in patients with ISR across different DES generations when follow-up less than one year and more than one year ($p > 0.05$) [13]. This may be due to the smaller sample size in our study compared to Kilickesmez's research.

With an odds ratio (OR) > 1, diabetes was associated with an increased risk of diffuse ISR compared to focal ISR, with corresponding rates of 50% and 46.7%. However, this difference was not statistically significant ($p < 0.05$). In comparison, the study by Park et al. examining predictors of diffuse ISR after DES placement in 159 patients found no significant difference in the prevalence of diabetes between the diffuse ISR group (28.7%) and the focal ISR group (19.6%) ($p = 0.221$) [14]. Other factors, such as female sex and kidney failure, were less common in the focal ISR group compared to the diffuse ISR group, with corresponding rates of 30% vs. 35% for females ($p > 0.05$) and 36.7% vs. 42.5% for kidney failure ($p > 0.05$). The differences were not statistically significant, likely due to the small sample size and the fact that the majority of our chronic kidney disease patients had mild to moderate glomerular filtration rate (mean glomerular filtration rate 73.33 ± 19.07), therefore the difference between these 2 groups was not statistically significant.

The prevalence of dyslipidemia in the diffuse ISR group (77.5%) was significantly higher than in the focal ISR group (50%) ($p < 0.05$). Univariate regression analysis indicated that dyslipidemia increased the risk of diffuse ISR, with an OR of 3.44 (95% confidence interval [CI]: 1.23 - 9.66, $p < 0.05$).

Lesion length was also associated with an increase in the mean lumen diameter by 0.58% for each millimeter of lesion with regression coefficient of 0.58 (95% CI: 0.19-0.97, $p < 0.05$). Multivariate analysis showed that lesion length was the only factor increasing the mean lumen diameter by 0.49% per millimeter of lesion with regression coefficient of 0.49, (95% CI: 0.09-0.88, $p < 0.05$). In the study by Zhao et al., lesion length was an independent predictor of ISR after DES placement in patients with stable angina, with an OR of 2.01 (95% CI: 1.98-3.78, $p < 0.01$) [15].

While this study provides valuable insights into ISR risk factors, certain limitations should be acknowledged. The cross-sectional design prevents the establishment of causality between ISR and the identified risk factors, and the relatively small sample size may limit the generalizability of the findings. Furthermore, as a single-center study, the results may not fully represent broader patient populations. The follow-up period was also limited to two years post-PCI, meaning that the long-term effects of ISR and late restenosis require further investigation. Future research should address these limitations through larger, multi-center, and prospective studies with extended follow-up periods.

V. CONCLUSION

In-stent restenosis (ISR) remains a significant complication after PCI with drug-eluting stents (DES). This study identified lesion length, post-intervention vessel diameter, and first-generation DES as key factors associated with diffuse ISR. Comorbidities such as dyslipidemia and chronic kidney disease were linked to increased ISR severity. These findings underscore the need for optimized stent deployment, risk factor control, and multidisciplinary follow-up to reduce ISR rates and improve patient outcomes. Further prospective studies are needed to validate these results and refine prevention strategies.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Hue Central hospital.

Competing interests

The authors declare that they have no competing interests.

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