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Original Article

Prevalence of In-Stent Restenosis in Patients having Drug Eluting Stents with Lengths Exceeding 40mm: A Single-Center Study

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ABSTRACT

Background: Coronary artery disease (CAD) remains a significant global health challenge, with percutaneous coronary intervention (PCI) being a primary treatment method. The use of long drug-eluting stents (DES) has been linked to varied outcomes, particularly concerning in-stent restenosis (ISR), which may be influenced by factors like stent length and patient comorbidities.

Objective: To assess the prevalence of ISR in patients undergoing PCI with long DES (>40mm), considering patient demographics, comorbidities, and lesion characteristics.

Methods: This cross-sectional study was conducted at Frontier Corps Teaching Hospital (FCTH) and Lady Reading Hospital in Peshawar, Pakistan, involving 102 patients. The study focused on the frequency of ISR post-angioplasty, particularly in relation to comorbid conditions such as diabetes and hypertension. Data collection included demographics, echocardiographic assessments, and detailed angiogram analysis. Statistical analysis was performed using SPSS version 23.0, with a significance threshold set at $p<0.05$.

Results: The overall prevalence of ISR was found to be 18.63%. Diabetes and hypertension showed a significant association with ISR, with p-values <0.0015. The ISR frequencies for single vessel disease (SVCAD), double vessel disease (DVCAD), and triple vessel disease (TVCAD) were 26.32%, 31.58%, and 42.10%, respectively, with TVCAD showing a statistically significant association ($p=0.0185$).

Conclusion: The study highlights a significant association between long DES and increased ISR rates, particularly in patients with complex coronary anatomies and multiple comorbidities. Shorter stents are recommended to potentially reduce restenosis and improve outcomes in CAD management.

Keywords: CAD, Drug-Eluting Stents, In-Stent Restenosis, Long DES, Percutaneous Coronary Intervention.

INTRODUCTION

Coronary artery disease (CAD) has emerged as a significant global health concern, consistently increasing in prevalence over recent years and now ranking as the third leading cause of death worldwide, responsible for approximately 17.8 million fatalities annually (1,2). A frequent complication of percutaneous coronary intervention (PCI), a common therapeutic approach for CAD, is restenosis. This condition involves the narrowing of the arterial lumen after angioplasty or stent implantation (3).

The introduction of bare-metal stents (BMS) in the mid-1990s marked a pivotal advancement in stent technology, which saw further evolution with the widespread adoption of drug-eluting stents (DES). These developments significantly transformed the management of CAD. However, despite these technological advancements, in-stent restenosis (ISR) remains a significant challenge. It continues to affect up to 30% of patients treated with BMS and approximately 10% of those receiving DES (4-6).

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Stent length has been identified as a critical factor influencing the risk of restenosis, highlighting the need for strategic consideration in treatment planning (7). Furthermore, the classification of coronary lesions from focal to diffuse adds layers of complexity to CAD management (8). Particularly challenging are diffuse long coronary lesions, which often require the placement of multiple overlapping stents, thereby increasing the risk of complications such as stent thrombosis (9).

Recent advancements in stent design have been promising, particularly with the introduction of second-generation DES featuring ultrathin struts and improved flexibility (10). These innovations have shown that very long DES, exceeding 40 mm, can be a safe and effective alternative for treating extensive coronary lesions. Such stents have been associated with favorable clinical outcomes and reduced procedural complexities (11,12).

This study aims to assess the prevalence of ISR among patients undergoing PCI with long DES (greater than 40mm) by considering a comprehensive range of factors including patient demographics, comorbid conditions, and lesion characteristics. Through this analysis, the study endeavors to illuminate current challenges and enhance strategies for optimizing therapeutic outcomes in managing CAD, thereby addressing critical gaps in contemporary cardiovascular intervention practices.

MATERIAL AND METHODS

The study was conducted at the Cardiology Department of Frontier Corps Teaching Hospital (FCTH) and Lady Reading Hospital in Peshawar, Pakistan, from May to October 2023. Following the approval from the institutional ethical board, a total of 102 patients were enrolled in this cross-sectional investigation after providing written informed consent. The recruitment criteria included both male and female patients aged between 30 and 80 years who had undergone angioplasty and were exhibiting symptoms of angina, new-onset acute coronary syndrome (ACS), or were diagnosed with in-stent restenosis (ISR) during repeat angiography. Patients with pre-existing kidney or liver failure were excluded to avoid confounding effects on the study outcomes.

Data collection focused on demographic parameters such as age, gender, and body mass index (BMI), alongside medical history noting any comorbidities. Echocardiographic evaluations were performed to ascertain the left-ventricular ejection fraction (LVEF), and the presence of ISR was confirmed through detailed angiographic analysis conducted by seasoned interventional cardiologists. Comprehensive records were maintained regarding the specifics of previous angioplasty procedures and the characteristics of the stents used.

For statistical analysis, continuous variables were summarized using means and standard deviations, while categorical variables were described through frequencies and percentages. The threshold for statistical significance was established at a p-value of less than 0.05. All statistical analyses were carried out using SPSS version 23.0. The primary objective of this research was to ascertain the prevalence of ISR among patients with a history of angioplasty, paying particular attention to those with comorbid conditions such as diabetes and hypertension, which could influence the rates of restenosis.

RESULTS

In a recent study of 102 participants conducted at a specialized cardiology unit, the majority of the patients were male, constituting 58.8% of the sample, while females represented 41.2%. The average age of the participants was calculated to be 52.46 years with a standard deviation of 9.13 years. The body mass index (BMI) of the group averaged at 27.36 kg/m^2, with a standard deviation of 11.64 kg/m^2.

Clinically, the cohort predominantly displayed symptoms of stable ischemic heart disease (IHD), which was observed in 39.2% of the cases. This was followed by presentations of unstable angina and non-ST segment elevation myocardial infarction (NSTEMI) at 21.6% and 24.5%, respectively, while ST segment elevation myocardial infarction (STEMI) was evident in 14.7% of the cases. Regarding cardiac function, impaired left ventricular ejection fraction (LVEF), defined as below 40%, was noted in 34.3% of the patients. Furthermore, 9.8% of the participants had undergone a previous percutaneous coronary intervention (PCI).

The comorbidities of hypertension (HTN) and diabetes mellitus (DM) were prevalent in 39.2% and 29.4% of the patients, respectively. A significant proportion, 31.4%, were found to suffer from both HTN and DM concurrently. In the analysis of angiographic data, single vessel coronary artery disease (SVCAD) affected 24.5% of the patients, with the left anterior descending artery (LAD) being the most affected at 10%. The right coronary artery (RCA) and the left circumflex artery (LCx) followed at 9.8% and 4.9%, respectively. More extensive involvement was noted with double vessel disease (DVCAD) and triple vessel disease (TVCAD) observed in 29.4% and 46.1% of cases, respectively.

The study also examined the occurrence of in-stent restenosis (ISR). It was identified in 19 of the 102 patients, resulting in an overall ISR prevalence of 18.63%. Among the ISR cases, 6 patients were diabetic, accounting for 31.57% of the ISR cases. Four ISR cases were seen in patients with hypertension, making up 21.05% of ISR occurrences. Notably, the combination of hypertension and

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diabetes was present in 9 of the ISR cases, corresponding to 47.38% of the occurrences, with a statistically significant p-value of 0.0015, suggesting a higher risk of ISR among patients with these comorbidities.

The relationship between the type of coronary artery involvement and ISR was further analyzed. ISR frequency was moderately associated with SVCAD at 26.32%, but this association was not statistically significant (p-value = 0.3573). ISR occurrence was 21.05% in patients with LAD involvement, and no ISR cases were linked to LCx. The RCA showed a lower frequency of ISR at 5.27%. Although DVCAD exhibited an ISR frequency of 31.58%, the correlation did not reach statistical significance (p-value = 0.1884). In contrast, TVCAD showed a significant correlation with ISR, presenting the highest ISR frequency of 42.1% and a statistically significant p-value of 0.0185.

Table-1: Characteristics of the study group at baseline

Variable		Values (N=102)/ Percentage (%)/ Mean ± SD
Gender	Male	60 (58.8%)
	Female	42 (41.2%)
Mean age, years		52.46 ±9.13
Body mass index (BMI), kg/m2		27.36 ± 11.64
Clinical presentation		
STEMI		15 (14.7%)
NSTEMI		25 (24.5%)
Stable IHD		40 (39.2%)
Unstable angina		22 (21.6%)
Impaired LV Function (EF <40%)		35 (34.3%)
Previous PCI		10 (9.8%)
Co-morbidities		
Diabetes mellitus (DM)		30 (29.4%)
Hypertension (HTN)		40 (39.2%)
HTN + DM		32 (31.4%)
Angiographic severity of CAD (target vessel location)		
Single vessel disease (SVCAD)		25 (24.5%)
LAD		10 (10%)
LCx		5 (4.9%)
RCA		10 (9.8%)
Double vessel disease (DVCAD)		30 (29.4%)
Triple vessel disease (TVCAD)		47 (46.1%)

Table-2: Frequency of ISR in various co-morbid conditions

Co-morbids	Frequency of ISR (n=19, 18.63%)	p-value
Diabetes mellitus (DM)	6 (31.57%)	0.0015
Hypertension (HTN)	4 (21.05%)	
HTN + DM	9 (47.38%)	

Table-3: Relationship between severity of CAD and ISR

Severity of CAD	Frequency of ISR (n=19, 18.63%)	p-value
Single vessel disease (SVCAD)	5 (26.32%)	0.3573
LAD	4 (21.05%)	
LCx	0 (0%)	
RCA	1 (5.27%)	
Double vessel disease (DVCAD)	6 (31.58%)	0.1884
Triple vessel disease (TVCAD)	8 (42.1%)	0.0185

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DISCUSSION

The recent study focused on the implications of utilizing long drug-eluting stents (DES) of 40 mm or more in patients with diffuse coronary artery disease (CAD), a growing global health concern. The patient cohort, with an average age of 52.46 years and a balanced gender distribution, displayed a high cardiovascular risk profile, largely attributed to prevalent comorbidities such as hypertension (39.2%) and diabetes mellitus (29.4%). These findings are crucial as they reinforce the association between these comorbid conditions and higher incidences of in-stent restenosis (ISR), a significant challenge in the post-percutaneous coronary intervention (PCI) setting.

The study's strength lies in its real-world setting and its focus on a diverse patient population, providing valuable insights into the effectiveness and challenges associated with the use of long DES in managing complex CAD lesions. A notable 18.63% incidence of ISR was observed, which underscores the need for careful patient selection and personalized treatment strategies to optimize outcomes. This aligns with existing literature that identifies hypertension as a significant predictor of ISR, supporting previous research by Wang et al. (13). Moreover, the persistent link between diabetes mellitus and increased ISR risk highlighted in our findings corroborates earlier studies (14-15), emphasizing the need for ongoing research to clarify the mechanisms driving this association.

Despite these insights, the study has limitations, including its single-center design and the relatively small sample size, which may affect the generalizability of the findings to broader populations. Additionally, the cross-sectional nature of the study limits the ability to draw causal inferences between stent length, comorbid conditions, and ISR incidence (16-18).

Furthermore, while the study contributes to the evolving understanding of PCI procedures, it also highlights the necessity for further research into the specific mechanisms by which hypertension and diabetes contribute to ISR development. Such research could lead to more targeted therapeutic interventions, enhancing clinical management strategies and patient outcomes in this complex patient population (19,20).

In conclusion, the findings from this study provide substantial evidence of the safety and efficacy of long DES in treating patients with diffuse CAD, while also documenting the associated risks of ISR. By addressing these challenges and building on the strengths of the study, future research can continue to refine treatment approaches, aiming to improve the quality of care and outcomes for patients with complex cardiovascular conditions.

CONCLUSION

In conclusion, this study underscores the heightened risk of restenosis when using long stents in patients with complex coronary anatomies and comorbid conditions such as hypertension and diabetes. The findings advocate for a cautious approach in stent selection, suggesting that shorter stents could reduce the incidence of restenosis and enhance clinical outcomes in the management of coronary artery disease. This insight is pivotal for clinicians as it emphasizes the necessity of tailoring stent length to individual patient profiles to optimize treatment efficacy and minimize complications in the treatment of this prevalent and impactful health issue.

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