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Identification Of Risk Factors Influencing In-Stent Restenosis (ISR) In Post Percutaneous Coronary Intervention (PCI) Patients.

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Abstract

Background: To identify and analyze the risk factors influencing in-stent restenosis (ISR) in patients following percutaneous coronary intervention (PCI).

Methodology: A retrospective cross-sectional study was conducted at the Cardiology Unit of Hayat Abad Medical Complex, Peshawar, from February 2021 to September 2022. The study included 292 patients who had undergone PCI within the last six years and were currently presenting with symptoms of angina or acute coronary syndrome (ACS). Patients were divided into two groups based on coronary angiography findings: ISR Group (n=147) and Non-ISR Group (n=145). Data collection was performed using a pre-designed questionnaire, with subsequent clinical and laboratory examinations to identify potential ISR risk factors. Statistical analysis involved chi-square and t-tests for categorical and continuous variables, respectively, and multivariate logistic regression to adjust for confounders.

Results: Significant risk factors for ISR included diabetes mellitus (P=0.001), smoking (P=0.002), hypertension (P=0.003), and elevated LDL cholesterol levels (P=0.030). Stent-related factors such as longer stent length (>40mm) and smaller diameter (<2.75mm) also showed significant associations with ISR occurrence. The logistic regression analysis confirmed these factors as independent predictors of ISR.

Conclusion: The study highlights the importance of comprehensive risk factor management and careful procedural planning in reducing the incidence of ISR. Targeted interventions focusing on modifiable risk factors and optimizing stent selection and placement are crucial for improving long-term outcomes in patients undergoing PCI.

Keywords

In-stent restenosis (ISR), PCI, Risk factors, Coronary Angiography, Diabetes Mellitus, Hypertension.

Introduction

In-stent restenosis (ISR) represents a significant challenge in the management of coronary artery disease (CAD) following percutaneous coronary intervention (PCI). This complex phenomenon, where narrowing reoccurs within a stent post-implantation, demands a thorough understanding of its associated risk factors to enhance treatment outcomes and patient quality of life. Recent research has spotlighted several critical factors influencing ISR, thus aiding in the refinement of prevention and management strategies. For instance, Zimbakov et al. highlighted that diabetes, hyperlipidemia, and smoking are pivotal in elevating ISR risk, further compounded by the physical characteristics of the stent itself, such as type, size, and length[1]. Similarly, Gong Cheng et al. identified elevated postoperative levels of hs-CRP and HCY, as well as specific procedural aspects like coronary bifurcation lesions and stent length, as significant contributors to ISR[2]. Moreover, Alexandrescu et al. expanded on these findings by associating ISR with systemic conditions such as hypertension and chronic kidney disease (CKD), alongside procedural variables like multi-stenting and stent inflation pressure[3]. Such studies underscore the multifactorial nature of ISR, where both patient-specific and procedural variables intertwine.

Continuing from earlier studies, recent research provides an expanded understanding of the predictors and mechanisms of in-stent restenosis (ISR), broadening the scope to include both traditional and novel factors. M. K. Akboga et al. bring attention to the influence of systemic inflammatory markers such as neutrophil-to-lymphocyte ratio and the CHA2DS2-VASc score on ISR after drug-eluting stent implantation. Their work underlines the intricate relationship between systemic inflammation, lipid profiles, and ISR, suggesting that variables like statin adherence also play a crucial role in patient outcomes[4].

Further extending this discussion, Ming Yi et al. focus on the elderly with type 2 diabetes, emphasizing the critical impact of metabolic control on ISR risks. Their findings highlight the importance of managing blood glucose fluctuations and other metabolic parameters to mitigate ISR in this vulnerable population[5]. Moreover, Martino Pepe et al. explore the intersection of autoimmune diseases and ISR, positing that autoimmune-induced endothelial dysfunction significantly contributes to ISR. Their findings suggest potential therapeutic avenues, such as the use of methotrexate and anti-tumor necrosis factor treatments, to address this specific risk factor[6]. Adding a unique perspective, Ling Zhang et al. examine the role of infectious diseases, specifically syphilis, in ISR among CAD patients. Their study indicates that syphilis, particularly with higher titers, increases ISR risk, while effective antisyphilitic treatment serves as a protective factor[7].

Finally, Jiayu Zhao et al. contribute to the predictive modeling of ISR in patients treated with sirolimus-eluting stents. Their research establishes a model that incorporates various clinical and procedural factors, offering a tool with significant predictive accuracy for ISR[8].

These studies collectively enhance our understanding of ISR by integrating diverse biomedical and clinical factors. This broader perspective is crucial for developing targeted interventions and personalized management strategies to effectively address the multifaceted nature of ISR in patients undergoing PCI.

Methodology

Study Design: This study employed a retrospective cross-sectional design to investigate the risk factors influencing in-stent restenosis (ISR) in post-percutaneous coronary intervention (PCI) patients. The research was conducted at the Cardiology Unit of Hayat Abad Medical Complex (HMC), Peshawar, spanning from February 2021 to September 2022.

Study Population: The study cohort consisted of 292 patients who had previously undergone PCI within the last six years and were currently presenting with symptoms of angina or acute coronary syndrome (ACS). These patients were

classified into two groups based on their coronary angiography findings: the ISR Group (n=147) and the Non-ISR Group (n=145).

Sampling Technique: Participants were selected using a non-probability consecutive sampling method. This approach was chosen due to its effectiveness in capturing a continuous stream of cases, providing a comprehensive snapshot of the patient population during the study period.

Data Collection: Data collection was facilitated through a pre-designed questionnaire, which was administered after obtaining informed consent from each participant. The questionnaire was structured to gather detailed clinical and paraclinical information that might indicate potential risk factors for ISR.

Clinical and Laboratory Examinations: All patients underwent thorough clinical and laboratory examinations as part of their standard care. These assessments were aimed at identifying and documenting various clinical and paraclinical variables that could potentially contribute to the development of ISR.

Inclusion Criteria:

Gender: Both male and female patients were included in the study.

Age: Patients aged between 30 and 75 years were eligible.

Medical History: Only patients with a new diagnosis of angina or ACS, who had undergone angioplasty within the preceding six years, and whose new angiography confirmed ISR, were included in the study.

Exclusion Criteria:

Chronic Kidney Disease: Patients suffering from chronic kidney diseases were excluded from the study to avoid confounding effects on ISR due to renal impairment.

Ethical Considerations: The study was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. Ethical approval for the study was obtained from the relevant ethical committees at Hayat Abad Medical Complex (HMC), ensuring that all procedures performed were part of the standard care and complied with ethical norms.

Statistical Analysis: Statistical tests such as Chi-square and Fisher's exact tests were applied to categorical variables, while independent t-tests were used for continuous variables. Multivariate logistic regression adjusted for confounders to identify independent predictors of ISR, confirming the significant impact of identified clinical, paraclinical, and procedural factors.

Results

The results presents the findings of the study which aimed to identify risk factors associated with in-stent restenosis (ISR) in patients following percutaneous coronary intervention (PCI). The data were collected from 292 patients categorized into two groups based on ISR occurrence, analyzed via clinical and paraclinical evaluations.

Participant Demographics and Baseline Characteristics: The participants divided into the ISR Group (n=147) and the Non-ISR Group (n=145). The demographic and baseline clinical characteristics were balanced between the two groups. Most participants were males (65%), with an average age of 58 years, highlighting a gender disparity common in cardiovascular studies.

Key Findings: The analysis revealed significant differences in several clinical and paraclinical factors between the ISR and Non-ISR groups. Key risk factors such as smoking, hypertension, and diabetes mellitus showed a higher prevalence in the ISR Group. Elevated LDL cholesterol and inflammatory markers like C-reactive protein were also notably higher among ISR patients.

Table 1: Summary of Clinical & Para Clinical Risk Factors Associated with ISR

Variable	ISR Group (N=147)	Non-ISR Group (N=145)	P Value	Rr	95% Ci
Sex					
Male	96	92	0.989		
Female	51	53	0.522		
Age ≥ 50 Years	77	64	0.125		
Current Smokers	29	10	0.002	2.8	1.44 – 5.65
Hypertension	72	46	0.003	1.5	1.15 – 2.06
Diabetes Mellitus	68	40	0.001	1.6	1.22 – 2.30
Obesity	35	27	0.28	1.27	0.81 – 1.99
LDL Cholesterol > 90 Mg/Dl	53	36	0.03	1.45	1.01 – 2.07

Stent and Coronary Related Factors

Stent characteristics such as length and diameter, as well as procedural aspects like the presence of bifurcation lesions and the use of multiple stents, were significantly associated with ISR occurrences**.**

Table 2: Summary of Stent & Coronary Related Factors Associated with ISR

Variable	ISR Group (n=147)	Non-ISR Group (n=145)	P Value
Stent Length > 40mm	44	28	0.001
Stent Diameter > 3.5 mm	19	9	0.05
Stent Diameter < 2.75 mm	33	19	0.04
Bifurcation Lesions	30	14	0.01
Multiple Stents	59	40	0.02
CTO PCI	18	7	0.03
Stent Type			
BMS	17	7	0.04
DES	140	138	0.052

Discussion

The findings from the current study on the risk factors influencing in-stent restenosis (ISR) in post-percutaneous coronary intervention (PCI) patients and compares these results with findings from prior research. A deeper examination into how these findings align or diverge from previous studies helps to position this study within the broader field of cardiovascular research.

One of the key findings from the current study highlighted the significant role of traditional cardiovascular risk factors such as diabetes mellitus, hypertension, smoking, and high LDL cholesterol levels in predicting ISR. These factors were associated with a higher incidence of ISR, as evidenced by their statistical significance and high relative risks.

The symptomatic ISR rate in our study population, while not explicitly stated earlier, would compare to other findings in the literature. For instance, the SAMMPRIS trial reported a symptomatic ISR rate of 4.3% in their patient cohort. Depending on the ISR rates identified in our study, this comparison could help gauge the efficacy of PCI procedures and ISR management in different settings or under different treatment protocols. The SAMMPRIS trial's rate provides a benchmark for evaluating improvements or the need for changes in clinical practices around stent placement[9].

Consistent with findings from other studies, our research supports the notion that larger residual stenosis post-stent placement is a critical predictor of ISR[10,11,12]. This study did not directly measure residual stenosis but noted the importance of stent characteristics such as length and diameter, which indirectly influence the adequacy of the arterial lumen post-procedure. The relationship between stent dimensions and residual stenosis could be inferred, suggesting that suboptimal stent deployment or selection based on the arterial anatomy could lead to higher ISR rates. This aligns with the broader literature which posits that residual stenosis greater than 30% is a strong predictor of restenosis due to the likelihood of under-treatment of the lesion.

The significant associations found between ISR and modifiable risk factors such as smoking and LDL cholesterol levels emphasize the potential benefits of lifestyle modifications and stringent post-PCI management. These findings suggest that rigorous control of blood lipid levels, along with smoking cessation programs, could substantially reduce the risk of ISR. Moreover, attention to precise stent placement and the choice of stent type, especially in complex lesions or in patients with diabetes, could mitigate the high risk of restenosis.

Conclusion

In conclusion, this study contributes valuable information to the body of knowledge on ISR, reinforcing the need for comprehensive risk factor management and meticulous procedural planning in the treatment of coronary artery disease via PCI. By addressing both the modifiable lifestyle factors and the technical aspects of stent placement, healthcare providers can significantly enhance patient outcomes and reduce the incidence of ISR. Future research should focus on the longitudinal assessment of ISR development and the effectiveness of targeted interventions based on the identified risk factors. Investigating the genetic predispositions and molecular mechanisms underlying ISR could also provide novel insights for personalized therapies. Furthermore, exploring the impact of newer stent technologies and advanced procedural techniques in reducing ISR rates would be invaluable.

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