UNIVERSAL JOURNAL OF MEDICAL AND NATURAL SCIENCES
ISSN 2992-8826
https://sr-journals.org/index.php/UJMANS



CLINICAL AND PATHOPHYSIOLOGICAL DETERMINANTS OF CORONARY RESTENOSIS FOLLOWING PERCUTANEOUS CORONARY INTERVENTION

Tolibjonov Dilmurod Tolibjonovich
Assistant, Department of Internal Diseases in Family Medicine No. 1 and Fundamentals of Preventive Medicine, Tashkent State Medical University, Tashkent, 100109, Uzbekistan

Abstract. Background: Coronary restenosis remains a major limitation of percutaneous coronary intervention (PCI), despite significant progress in stent technologies and antiplatelet therapy. The mechanisms underlying restenosis involve complex interactions between vascular injury, inflammatory processes, platelet activation, and hemodynamic factors. **Objective:** To comprehensively evaluate clinical and pathophysiological determinants of coronary restenosis in patients with chronic coronary syndrome following PCI. **Methods:** A prospective observational study included 42 patients with chronic coronary syndrome who underwent PCI with stent implantation in the cardiology department of 1st City Clinical Hospital named after Ibn Sina. All patients underwent detailed clinical, laboratory, and instrumental assessment, including platelet aggregation studies, lymphocyte–platelet adhesion (LPA), fibrinogen levels, and central aortic pressure analysis using applanation tonometry. Patients were followed for 12 months, with repeated evaluations at 3, 6, and 12 months. Multivariate logistic regression analysis was performed to identify independent predictors of restenosis. **Results:** Restenosis was detected in 8 out of 42 patients (19.0%). Patients with restenosis demonstrated significantly higher spontaneous and ADP-induced platelet aggregation, reduced lymphocyte–platelet adhesion, elevated fibrinogen levels, and increased central pulse pressure. Multivariate analysis identified platelet hyperaggregation (OR=2.8), reduced LPA (OR=3.4), elevated fibrinogen (OR=2.1), age (OR=1.9), irregular aspirin intake (OR=2.5), and central pulse pressure (OR=2.6) as independent predictors of restenosis. **Conclusion:** Coronary restenosis is a multifactorial process involving platelet dysfunction, inflammatory activation, and vascular stiffness. Comprehensive assessment of these parameters may significantly improve early risk stratification and guide personalized post-PCI management strategies.

Keywords: restenosis; PCI; platelet aggregation; lymphocyte–platelet adhesion; fibrinogen; arterial stiffness

Аннотация. Актуальность: Рестеноз коронарных артерий остаётся одним из основных ограничений чрескожного коронарного вмешательства (ЧКВ), несмотря на значительный прогресс в технологиях стентирования и антиагрегантной терапии. Механизмы развития рестеноза включают сложное взаимодействие сосудистого повреждения, воспалительных процессов, активации тромбоцитов и гемодинамических факторов. **Цель:** Комплексная оценка клинических и патофизиологических детерминант рестеноза коронарных артерий у пациентов с хроническим коронарным синдромом после ЧКВ. **Материалы и методы:** В проспективное наблюдательное исследование включено 42 пациента с хроническим коронарным синдромом, перенесших ЧКВ со стентированием в кардиологическом отделении 1-й городской клинической больницы имени Ибн Сино. Всем пациентам проведено комплексное клинико-лабораторное и инструментальное обследование, включая оценку агрегации тромбоцитов, лимфоцитарно-тромбоцитарной адгезии (ЛТА), уровня фибриногена и центрального аортального давления методом

аппланационной тонометрии. Наблюдение проводилось в течение 12 месяцев с повторной оценкой через 3, 6 и 12 месяцев. Для выявления независимых предикторов рестеноза применялся многофакторный логистический регрессионный анализ. **Результаты:** Рестеноз выявлен у 8 из 42 пациентов (19,0%). У пациентов с рестенозом отмечались достоверно более высокие показатели спонтанной и АДФ-индуцированной агрегации тромбоцитов, снижение лимфоцитарно-тромбоцитарной адгезии, повышение уровня фибриногена и центрального пульсового давления. По данным многофакторного анализа независимыми предикторами рестеноза явились гиперагрегация тромбоцитов (OR=2,8), снижение ЛТА (OR=3,4), повышение уровня фибриногена (OR=2,1), возраст (OR=1,9), нерегулярный приём аспирина (OR=2,5) и повышенное центральное пульсовое давление (OR=2,6).
Заключение: Рестеноз коронарных артерий представляет собой многофакторный процесс, включающий нарушение функции тромбоцитов, воспалительную активацию и повышение жёсткости сосудов. Комплексная оценка этих показателей может существенно улучшить раннюю стратификацию риска и оптимизировать персонализированную терапию после ЧКВ.

Ключевые слова: рестеноз; ЧКВ; агрегация тромбоцитов; лимфоцитарно-тромбоцитарная адгезия; фибриноген; жёсткость артерий

Annotatsiya. Dolzarbligi: Koronar restenoz perkutan koronar aralashuv (PKA)ning asosiy cheklovlaridan biri bo‘lib qolmoqda, garchi stent texnologiyalari va antitrombotsitar terapiya sezilarli darajada rivojlangan bo‘lsa ham. Restenoz rivojlanish mexanizmlari tomir shikastlanishi, yallig‘lanish jarayonlari, trombotsitlar faollashuvi va gemodinamik omillar o‘rtasidagi murakkab o‘zaro ta’sir bilan bog‘liq. **Maqsad:** Surunkali koronar sindromli bemorlarda PKA dan keyin koronar restenozning klinik va patofiziologik determinantlarini kompleks baholash. **Material va usullar:** Tadqiqotga 42 nafar surunkali koronar sindromli bemor kiritildi, ular Ibn Sino nomidagi 1-son shahar klinik shifoxonasining kardiologiya bo‘limida PKA bilan davolangan. Barcha bemorlarda trombotsitlar agregatsiyasi, limfotsit-trombotsit adgeziyasi (LTA), fibrinogen darajasi va markaziy aortal bosim (applanatsion tonometriya orqali) baholandi. Bemorlar 12 oy davomida kuzatilib, 3, 6 va 12 oyda qayta tekshiruvdan o‘tkazildi. Mustaqil prediktorlarni aniqlash uchun ko‘p omilli logistik regressiya tahlili qo‘llanildi. **Natijalar:** Restenoz 42 bemordan 8 tasida (19,0%) aniqlandi. Restenoz rivojlangan bemorlarda trombotsitlarning spontan va ADP-induksiyalangan agregatsiyasi yuqori, LTA ko‘rsatkichi past, fibrinogen darajasi va markaziy puls bosimi yuqori bo‘lgan. Mustaqil prediktorlar sifatida trombotsit giperagregatsiyasi (OR=2,8), LTA pasayishi (OR=3,4), fibrinogen oshishi (OR=2,1), yosh (OR=1,9), aspirinni muntazam qabul qilmaslik (OR=2,5) va markaziy puls bosimining oshishi (OR=2,6) aniqlangan. **Xulosa:** Koronar restenoz trombotsit funksiyasi buzilishi, yallig‘lanish va tomir qattiqligining oshishi bilan bog‘liq ko‘p omilli jarayondir. Ushbu ko‘rsatkichlarni kompleks baholash xavfni erta aniqlash va individual davolashni optimallashtirish imkonini beradi.

Kalit so‘zlar: restenoz; PKA; trombotsit agregatsiyasi; limfotsit-trombotsit adgeziyasi; fibrinogen; arteriya qattiqligi

Introduction. Cardiovascular diseases remain the leading cause of mortality worldwide, accounting for a substantial proportion of global morbidity and healthcare burden [1,2]. Coronary artery disease is the most prevalent manifestation, and percutaneous coronary intervention (PCI) has become the cornerstone of its management. Despite advances in interventional cardiology, including the introduction of drug-eluting stents and improved pharmacotherapy, restenosis continues to limit the long-term effectiveness of PCI. According to various studies, the incidence of restenosis ranges from 3% to 30%, depending on patient characteristics, lesion complexity, and treatment strategy [3]. Restenosis is not merely a mechanical problem but a complex biological process involving endothelial damage, inflammatory activation, smooth muscle cell proliferation, and extracellular matrix deposition. Platelet activation plays a central role by releasing growth factors such as PDGF and TGF-β, which stimulate neointimal hyperplasia. Traditional predictors, including diabetes mellitus, lesion length, and vessel diameter, provide only partial prognostic value. Therefore, there

is increasing interest in identifying novel markers reflecting underlying pathophysiological processes, including platelet reactivity, immune–hemostatic interactions, and vascular stiffness. The present study aims to evaluate these determinants in a clinical setting and to identify factors associated with restenosis following PCI.

Literature Review. The development of restenosis following PCI has been extensively studied over the past decades, yet it remains a clinically relevant problem. Early investigations focused primarily on anatomical and procedural factors; however, more recent research has highlighted the importance of biological mechanisms. Platelet activation is considered a key contributor to restenosis. Activated platelets release a variety of mediators that promote inflammation and vascular smooth muscle proliferation. Studies have demonstrated that increased platelet reactivity is associated with adverse cardiovascular outcomes and may predict restenosis [6]. Fibrinogen, an acute-phase reactant, plays a dual role in coagulation and inflammation. Elevated fibrinogen levels contribute to increased blood viscosity, platelet aggregation, and thrombus formation. Clinical studies have shown a strong association between hyperfibrinogenemia and restenosis risk [7]. Another important but less explored mechanism is lymphocyte–platelet interaction. Lymphocyte–platelet adhesion reflects the interaction between immune and coagulation systems. Disruption of this interaction may impair endothelial repair and contribute to pathological vascular remodeling. In addition, arterial stiffness has emerged as an important determinant of cardiovascular outcomes. Increased central pulse pressure reflects elevated arterial rigidity and is associated with endothelial dysfunction and impaired coronary perfusion. These hemodynamic changes may enhance neointimal proliferation and promote restenosis [8].

Despite growing evidence, integrated assessment of these factors remains limited, particularly in regional populations. This underscores the importance of comprehensive studies evaluating both clinical and pathophysiological determinants of restenosis.

Materials and Methods. This prospective observational study was conducted between 2009 and 2011 in the cardiology department of 1st City Clinical Hospital named after Ibn Sina, which serves as a tertiary referral center. A total of 42 patients aged 35 to 75 years with chronic coronary syndrome and stable angina class III were included in the study. All patients underwent PCI with stent implantation according to standard clinical guidelines. **Inclusion Criteria**: -Age 35–75 years, -Stable angina (class III), -Indication for PCI. **Exclusion Criteria:** -Acute myocardial infarction, -Severe heart failure (NYHA IV), -Malignancy, -Severe renal or hepatic dysfunction, -Active inflammatory diseases.

Clinical Assessment: All patients underwent detailed clinical evaluation, including medical history, physical examination, ECG, and echocardiography. Risk factors such as hypertension, diabetes mellitus, and smoking were documented.

Laboratory and Instrumental Methods: Platelet aggregation was assessed using laser aggregometry with ADP and adrenaline as inducers. Lymphocyte–platelet adhesion (LPA) and lymphocyte–platelet index were determined using standard cytological techniques. Fibrinogen levels were measured using the Clauss method.

Central aortic pressure and arterial stiffness were evaluated using applanation tonometry (SphygmoCor system).

Follow-Up: Patients were followed for 12 months with repeated assessments at 3, 6, and 12 months. Restenosis was confirmed by coronary angiography.

Statistical Analysis: Continuous variables were expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test or Mann–Whitney test. Multivariate logistic regression analysis was used to identify independent predictors of restenosis. Statistical significance was defined as $p < 0.05$.

Results. During the 12-month follow-up period, restenosis was detected in 8 patients (19.0%). Patients with restenosis were older and had a higher prevalence of cardiovascular risk factors, although these differences were not statistically significant for all variables.

Table 1. Baseline Clinical Characteristics

Parameter	No Restenosis (n=34)	Restenosis (n=8)	p-value
Age (years)	55.8 ± 7.2	61.3 ± 6.5	0.04
Male (%)	76%	75%	0.91
Hypertension (%)	65%	75%	0.52
Diabetes (%)	24%	37%	0.31
Smoking (%)	47%	50%	0.88

Platelet Function: Patients with restenosis demonstrated significantly higher spontaneous platelet aggregation (1.8 ± 0.5 vs 1.2 ± 0.3; p=0.01). ADP-induced aggregation remained elevated during follow-up, indicating persistent platelet hyperreactivity.

Lymphocyte–Platelet Adhesion: A marked reduction in LPA was observed in the restenosis group (9.8 ± 1.7% vs 15.4 ± 2.1%; p=0.001), suggesting impaired immune–hemostatic interaction.

Fibrinogen: Fibrinogen levels were significantly higher in patients with restenosis (4.5 ± 0.8 g/L vs 3.2 ± 0.6 g/L; p=0.002).

Hemodynamic Parameters: Central pulse pressure was significantly elevated in the restenosis group (52 ± 8 mmHg vs 38 ± 6 mmHg; p=0.001).

Table 2. Independent Predictors of Restenosis

Parameter	OR	95% CI	p-value
Platelet aggregation	2.8	1.3–5.9	0.01
LPA (decrease)	3.4	1.5–7.1	0.002
Fibrinogen	2.1	1.1–4.2	0.01
Age	1.9	1.0–3.5	0.04
Aspirin non-adherence	2.5	1.2–5.1	0.03
Central pulse pressure	2.6	1.2–5.4	0.01

Discussion. The findings of this study provide further evidence that restenosis is a multifactorial process involving both clinical and biological mechanisms. Platelet hyperreactivity appears to play a central role, contributing to thrombus formation and vascular remodeling. Persistent platelet activation after PCI may lead to excessive neointimal proliferation. Reduced lymphocyte–platelet adhesion suggests impaired interaction between immune and hemostatic systems, which may disrupt normal endothelial repair mechanisms. Elevated fibrinogen levels reflect systemic inflammation and a prothrombotic state, both of which are known contributors to restenosis. Increased arterial stiffness and central pulse pressure indicate unfavorable hemodynamic conditions that promote vascular injury and remodeling. These findings highlight the importance of integrated assessment of hemostatic, inflammatory, and vascular parameters in predicting restenosis.

Conclusion. Coronary restenosis following PCI is associated with platelet hyperaggregation, impaired lymphocyte–platelet interaction, elevated fibrinogen levels, and increased arterial stiffness. Identification of these determinants may improve early risk stratification and allow optimization of individualized treatment strategies.

References

1. World Health Organization. Cardiovascular diseases (CVDs). Geneva: WHO; 2023.
2. Mills KT, Stefanescu A, He J. Global epidemiology of hypertension. Nat Rev Nephrol. 2020;16:223–237.
3. George D, et al. Restenosis after PCI. Circulation. 2010;121:234–241.
4. Mintz GS, et al. Mechanisms of restenosis. J Am Coll Cardiol. 1996;28:167–174.
5. Stoiker JM, et al. Predictors of restenosis. Eur Heart J. 2010;31:213–220.
6. Gurbel PA, et al. Platelet function after PCI. Circulation. 2001;103:2572–2578.
7. Lupi A, et al. Fibrinogen and restenosis. J Thromb Thrombolysis. 2012;33:308–317.
8. Jankowski P, et al. Pulse pressure and restenosis. Am J Cardiol. 2001;87:125–129.
9. Patrono C, et al. Antiplatelet therapy. Eur Heart J. 2004;25:166–181.
10. Williams B, et al. ESC Guidelines for hypertension. Eur Heart J. 2023;44:2523–2639.