

# Pathogenetic Factors of Complications of Percutaneous Coronary Intervention (Restenosis and Stent Thrombosis)

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**Abstract** This article examines the main complications following percutaneous coronary intervention restenosis and stent thrombosis as well as their pathogenetic factors. The study was conducted based on a retrospective analysis of the medical records of 307 patients who underwent percutaneous coronary intervention in 2024 at the Andijan Branch of the Republican Specialized Scientific and Practical Medical Center of Cardiology. In the patients, inflammatory markers (CRP, fibrinogen), coagulation system parameters (PTI, thrombin time, aPTT, INR, platelet count), and lipid metabolism indicators (total cholesterol, low-density lipoprotein cholesterol) were evaluated. According to the results, disorders of inflammation, coagulation processes, and lipid metabolism were found to play a significant role in the development of restenosis and stent thrombosis.

**Keywords** Percutaneous coronary intervention, Restenosis, Stent thrombosis, Inflammatory markers, Lipid metabolism

## 1. Introduction

Today, percutaneous coronary intervention (PCI) is considered one of the most commonly used and effective methods in the treatment of ischemic heart disease. Nevertheless, a number of complications that arise after the intervention remain a major challenge in clinical practice. Among these, restenosis and stent thrombosis are the most frequent and life-threatening conditions. As noted in the literature, cases of restenosis after PCI often necessitate repeat interventions and reduce the overall effectiveness of treatment. In a large-scale network meta-analysis conducted by Siontis et al. (2015), the efficacy of different interventional strategies was compared, showing that drug-eluting stents and drug-coated balloons provide better clinical outcomes compared to conventional balloon angioplasty. However, despite the use of these approaches, restenosis has not been completely eliminated and remains a serious and relevant clinical problem. The presence of restenosis not only forces patients to seek repeated hospitalizations but also increases the risk of stent thrombosis. This, in turn, limits the long-term effectiveness of PCI and creates an additional economic burden for the healthcare system. Therefore, investigating the causes of restenosis and stent thrombosis after PCI and developing preventive measures are among the most

important and urgent directions of modern cardiology [1].

Despite the rapid development of percutaneous coronary intervention (PCI) technologies over the past two decades, restenosis and stent thrombosis continue to represent major limitations of this procedure. During the era of first-generation stents, the high rate of restenosis was a serious obstacle to the widespread use of PCI. In the subsequent stage, the introduction of drug-eluting stents significantly reduced the incidence of restenosis; however, their use was found to increase the risk of late stent thrombosis.

As Byrne et al. (2015) emphasized, although stent thrombosis occurs relatively rarely, its clinical consequences are extremely severe — in most cases resulting in acute myocardial infarction or sudden cardiac death. Therefore, in-depth investigation of the pathogenesis of restenosis and stent thrombosis after PCI, as well as the development of effective preventive and therapeutic strategies, remains one of the most pressing and unresolved issues in modern cardiology [2].

In order to reduce the incidence of restenosis after PCI, along with interventional technologies, pharmacological approaches have also been explored. In particular, the efficacy of probucol, a drug with antioxidant and lipid-lowering effects, has been investigated in several clinical studies. According to the results of a systematic review and meta-analysis conducted by Liu et al. (2015), treatment with probucol can significantly decrease the rates of restenosis. This finding highlights the important role of inflammatory and oxidative processes in the pathogenesis of restenosis after PCI. At the same time, the authors emphasize the need

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for additional large-scale studies before these results can be widely implemented in clinical practice. Thus, the problem of restenosis after PCI remains relevant not only from the interventional but also from the pharmacological prevention perspective, requiring a comprehensive approach to achieve long-term effectiveness in modern cardiology [3].

Over the past decades, percutaneous coronary intervention has developed at a rapid pace, becoming the leading technology in the treatment of ischemic heart disease. The introduction of modern drug-eluting stents has markedly increased the effectiveness of PCI and improved its short-term outcomes. As Rinfret *et al.* (2015) noted, PCI can be regarded as a “mature” method that has established a firm position in clinical practice. Nevertheless, cases of restenosis and stent thrombosis after intervention still persist as major clinical problems. They limit the long-term safety and efficacy of PCI and increase the need for repeat interventions in patients. Therefore, despite PCI reaching a stage of maturity, eliminating its major complications remains one of the pressing tasks of modern cardiology [4].

In-stent restenosis (ISR) is one of the most common problems after PCI, limiting clinical efficacy and creating the need for repeat interventions in patients. According to the results of a large-scale network meta-analysis conducted by Sethi *et al.* (2015), among various interventional strategies, drug-eluting stents and drug-coated balloons are considered the most effective methods. At the same time, conventional approaches remain less effective. As the authors emphasize, the optimal interventional strategy for ISR has not yet been fully determined, and decisions should take into account the patient’s individual clinical and anatomical characteristics. This underscores that the problem of restenosis after PCI has not been fully resolved and highlights the importance of further research and the search for new effective solutions [5].

Among the complications after PCI, stent thrombosis holds particular importance. Although it occurs relatively rarely, its clinical consequences are severe, most often leading to acute myocardial infarction or sudden cardiac death. In particular, in cases of rescue percutaneous intervention (rescue PCI) performed for STEMI, the risk of stent thrombosis has been reported to be higher (Thani *et al.*, 2015). As the authors point out, the development of thrombosis is influenced by multiple factors, including platelet activity, inflammatory processes, and the effectiveness of antiplatelet therapy. Therefore, stent thrombosis remains one of the most dangerous complications after PCI in clinical practice, and the need to improve strategies for its prevention and treatment remains an urgent priority [6].

In recent years, significant progress has been achieved in the field of PCI, with modern drug-eluting stents and drug-coated balloons being widely introduced into clinical practice. As noted by Grines *et al.* (2016), studies conducted in 2015 were aimed at further improving the efficacy and safety of PCI. However, complications such as restenosis and stent thrombosis still remain among the major challenges. Second- and third-generation drug-eluting stents have

reduced these risks to some extent, but the problem has not been completely resolved. It has been established that these complications have a multifactorial pathogenesis, in which inflammation, endothelial dysfunction, platelet activity, and metabolic factors play a key role. Therefore, restenosis and stent thrombosis after PCI continue to be one of the most urgent research areas in modern interventional cardiology [7].

One of the main complications after PCI — restenosis and stent thrombosis — poses serious challenges for physicians in clinical practice when making treatment decisions. Long-term antiplatelet therapy is used to prevent these conditions; however, this approach in turn increases the risk of bleeding. As Torrado *et al.* (2018) emphasized, physicians must strike a balance between preventing restenosis and stent thrombosis and avoiding an excessive increase in bleeding complications. This issue demonstrates that strategies for the prevention and treatment of PCI-related complications are still not fully optimized. Therefore, restenosis and stent thrombosis after PCI remain among the most relevant research directions in modern interventional cardiology [8].

Among the complications after PCI, early stent thrombosis is considered particularly dangerous. A patient-level analysis of two large clinical trials conducted by Dangas *et al.* (2016) demonstrated that in cases of early stent thrombosis, mortality rates increase sharply. This complication is most often associated with severe clinical manifestations of myocardial infarction and hemodynamic instability. The main risk factors for early thrombosis include PCI performed in the context of STEMI, high thrombus burden, technical difficulties, and insufficient antiplatelet therapy. Therefore, the prevention of early stent thrombosis remains one of the most important and urgent tasks in interventional cardiology [9].

Percutaneous coronary intervention has firmly established itself in cardiology practice as one of the most effective and widely used methods for the treatment of cardiovascular diseases. However, despite advances in stent generations and interventional technologies, restenosis and stent thrombosis after PCI continue to represent major challenges in clinical practice. It should be noted that restenosis is often associated with neointimal hyperplasia and pronounced biological responses, leading to the need for repeat interventions. Stent thrombosis, on the other hand, is a particularly dangerous complication, with its early forms significantly increasing mortality in the context of STEMI. Moreover, interruption or insufficient administration of antiplatelet therapy, technical issues, and high thrombus burden further exacerbate these events.

Large-scale clinical studies indicate that, despite the use of modern drug-eluting stents, additional pharmacological strategies, and individualized antiplatelet therapy, these complications continue to limit the long-term effectiveness and safety of PCI. Therefore, the causes, pathogenesis, prevention, and effective treatment strategies of restenosis, stent thrombosis, and myocardial infarction after PCI remain among the most important and pressing areas of modern interventional cardiology.

**Research Objective:** The aim of this study is to analyze the causes of the main complications after percutaneous coronary intervention, namely restenosis and stent thrombosis, based on scientific sources; to investigate their pathogenetic mechanisms; and to substantiate effective approaches to prevention and treatment within the framework of modern interventional and pharmacological strategies.

## 2. Materials and Methods

Within the scope of the study, a retrospective analysis was performed on the medical records of 307 patients who underwent percutaneous coronary intervention during 2024 at the Andijan Branch of the Republican Specialized Scientific and Practical Medical Center of Cardiology. The mean age of the patients was  $58.2 \pm 9.3$  years, of whom 57% were men and 43% were women. The following laboratory parameters were evaluated:

- Inflammatory markers: C-reactive protein (CRP), fibrinogen;
- Coagulation system indicators: prothrombin index, thrombin time, activated partial thromboplastin time (aPTT), international normalized ratio (INR), platelet count;
- Lipid metabolism markers: total cholesterol and low-density lipoprotein cholesterol (LDL-C).

During statistical analysis, comparative evaluations were carried out between patient groups. Student's t-test was applied to assess continuous variables, while the  $\chi^2$  (chi-square) test was used for categorical indicators. Pearson's correlation coefficient was calculated to evaluate associations between variables. All calculations were performed using SPSS version 26.0 (IBM, USA). Results were expressed as mean  $\pm$  standard deviation. A p-value of  $<0.05$  was considered statistically significant.

## 3. Results

In 2024, the clinical and laboratory parameters of 307 patients who underwent PCI at the Andijan Branch of the Republican Specialized Scientific and Practical Medical Center of Cardiology were analyzed.

**Demographic characteristics:** The mean age of the patients was  $58.2 \pm 9.3$  years. Males accounted for 57% ( $n=175$ ) and females for 43% ( $n=132$ ). Analysis by age categories showed that the majority of patients were in the 50–65-year age range. **Inflammatory markers:** C-reactive protein (CRP) levels were elevated in the majority of patients. Higher CRP levels were associated with increased incidence of stent thrombosis and restenosis ( $p < 0.05$ ). Fibrinogen levels also demonstrated a significant association with post-PCI restenosis. **Coagulation system indicators:** Deviations from normal values in the prothrombin index and international normalized ratio (INR) were observed in 27% of patients. Shortened activated partial thromboplastin time (aPTT)

was more frequently detected in patients at higher risk of thrombotic complications ( $p < 0.05$ ). Elevated platelet counts were significantly associated with higher rates of stent thrombosis. **Lipid metabolism markers:** Most patients exhibited elevated levels of total cholesterol and low-density lipoprotein cholesterol (LDL-C). Lipid metabolism disorders were significantly correlated with restenosis development ( $r = 0.41$ ;  $p < 0.01$ ). **Clinical outcomes:** During follow-up after PCI, restenosis was identified in 12.4% of patients and stent thrombosis in 4.8%. Complications occurred more frequently among patients with elevated inflammatory markers and coagulation abnormalities. An unfavorable lipid profile, particularly elevated LDL, doubled the risk of restenosis (OR = 2.1; 95% CI: 1.4–3.2).

Statistical analysis confirmed these associations: according to the  $\chi^2$  test, patients with elevated CRP had twice the incidence of restenosis compared to those with normal CRP ( $\chi^2 = 6.47$ ;  $p = 0.011$ ). A significant correlation was found between prothrombin index, platelet count, and stent thrombosis ( $r = 0.36$ ;  $p = 0.02$ ). Pearson correlation analysis demonstrated a moderate positive association between lipid levels and restenosis ( $r = 0.41$ ;  $p < 0.01$ ).

## 4. Discussion

The results of this retrospective study demonstrated that multiple pathogenetic factors contribute to the development of restenosis and stent thrombosis following PCI. In particular, inflammatory markers (C-reactive protein, fibrinogen), coagulation system parameters, and lipid metabolism disorders were found to be of clinical significance.

First, the role of inflammation should be emphasized. Elevated levels of C-reactive protein and fibrinogen were found to be associated with restenosis. Previous studies (Byrne et al., 2015; Torrado et al., 2018) have also reported that endothelial injury after PCI enhances the inflammatory response, thereby accelerating neointimal hyperplasia. Our findings support this concept. Thus, regular monitoring of inflammatory biomarkers may serve as an important tool in assessing the risk of restenosis.

Second, the findings related to coagulation parameters are of particular importance. Alterations in the prothrombin index and activated partial thromboplastin time were statistically associated with stent thrombosis. This suggests that increased platelet aggregation and hypercoagulability are among the key mechanisms underlying post-PCI complications. Prior studies (Dangas et al., 2016; Thani et al., 2015) have similarly noted that early thrombosis often results from insufficient anticoagulant therapy and individual hemostatic characteristics of patients. Our results further confirm these observations.

Third, disorders of lipid metabolism—particularly elevated total cholesterol and low-density lipoprotein cholesterol—were shown to have a strong association with restenosis. This indicates that atherogenic dyslipidemia is a major factor contributing to adverse post-PCI outcomes.

Meta-analyses (Liu *et al.*, 2015; Sethi *et al.*, 2015) likewise demonstrated that effective lipid control significantly reduces the recurrence of restenosis.

In our study, restenosis was more frequently observed in patients with lipid profile abnormalities, whereas stent thrombosis was more often linked to coagulation disturbances. This highlights the predominance of different pathogenetic pathways in these two complications. Therefore, post-PCI assessment should not rely solely on clinical manifestations but should also incorporate a comprehensive evaluation of inflammatory, hemostatic, and lipid metabolism markers.

Our findings indicate that reducing post-PCI complications requires the following approaches:

- Monitoring inflammatory biomarkers and developing individualized therapeutic strategies to suppress inflammation;
- Individualized assessment of coagulation status with optimization of antiplatelet and anticoagulant therapy;
- Effective correction of lipid metabolism, particularly timely use of statins and novel lipid-lowering agents.

Overall, the study demonstrated that restenosis and stent thrombosis after PCI are multifactorial processes, with pathogenesis closely linked to inflammation, coagulation, and lipid metabolism. These insights emphasize the need for individualized risk assessment and the development of targeted prevention strategies in clinical practice.

## 5. Conclusions

According to the study results, restenosis and stent thrombosis after percutaneous coronary intervention are predominantly associated with inflammatory processes, coagulation system disorders, and atherogenic dyslipidemia. Furthermore, regular monitoring of inflammatory markers, coagulation parameters, and lipid profile indicators, as well as the individualization of treatment strategies, are considered crucial for the prevention of these complications.

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