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Research Article

Outcomes of Dual Antiplatelet Therapy beyond One Year in Patients Post-Drug Eluting Stent Placement: A Cohort Study

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Abstract

Introduction: The long-term use of Platelet Aggregation Inhibitors following Drug-Eluting Stent implantation is essential to prevent Stent Thrombosis and reduce the risk of Major Adverse Cardiovascular Events (MACE), but it may also increase the incidence of Hemorrhagic Complications, particularly with extended Dual Antiplatelet Therapy (DAPT). The study aimed to evaluate the outcomes of prolonged DAPT beyond one year in patients who had undergone Drug-Eluting Stent (DES) implantation, with a focus on MACE, Hemorrhage, and the influence of Comorbidity profiles on these outcomes.

Materials and Methods: This Cohort Study was conducted at the Hayatabad Medical Complex Peshawar and Rehman Medical College Peshawar over 12 months. A total of 110 patients who received DES and continued DAPT for more than one year were enrolled. Data were collected on Demography, Comorbidity, Platelet Aggregation Inhibitors, and cardiovascular outcomes. Descriptive Statistics, Chi-Square Distribution, and Logistic Models were used to analyze the data.

Results: The incidence of MACE was 18 (16.4%), with Myocardial Infarction and Revascularization of the target lesion being the most frequent events. Hemorrhagic Events were also reported in 18 patients (16.4%), including 5 (4.5%) with major bleeding and 13 (11.8%) with minor bleeding. Patients with Chronic Kidney Disease (CKD) had an increased but not statistically significant risk for MACE (Hazard Ratio = 2.3; 95% Confidence Interval: 0.91–5.79; p = 0.072). No significant difference in outcomes was observed between Aspirin + Clopidogrel and Aspirin + Ticagrelor therapy groups.

Conclusion: Extended use of DAPT beyond one year following DES implantation is associated with reduced cardiovascular events and acceptable hemorrhagic risk. CKD may contribute to increased adverse outcomes, warranting further studies with larger sample sizes and longer follow-up periods

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Introduction

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide [1]. Percutaneous coronary intervention (PCI), often accompanied by the implantation of drug-eluting stents (DES), has revolutionized the management of obstructive coronary lesions by significantly reducing the need for repeat revascularization [2]. Despite these advances, post-procedural complications such as in-stent thrombosis and major adverse cardiovascular events MACE continue to pose substantial risks to long-term patient outcomes [3].

To mitigate these risks, DAPT typically a combination of aspirin and a P2Y12 inhibitor is recommended following DES implantation [4]. While short-term DAPT (up to 12 months) has been well-established in clinical practice for reducing thrombotic complications, the role of extended DAPT beyond one year remains a subject of ongoing clinical investigation and debate. Prolonged therapy may provide continued protection against ischemic events; however, it also increases the risk of bleeding, raising important questions about the net clinical benefit in different patient subgroups [5].

Current international guidelines recommend tailoring DAPT duration based on individual risk profiles, balancing ischemic protection with the risk of hemorrhagic complications [6]. Tools such as the DAPT and PRECISE-DAPT scores are increasingly used to guide clinicians in this decision-making process [7]. Yet, these tools have limitations and may not fully capture the unique characteristics of all patients, particularly those from underrepresented regions [8]. Moreover, factors such as patient adherence, affordability of prolonged therapy, comorbidities (like diabetes or renal dysfunction), and procedural complexity add further layers of clinical complexity [9]. As a result, the decision to continue DAPT beyond one year often varies significantly in routine clinical practice, underscoring the need for more robust, context-specific evidence [10].

Recently DAPT, PEGASUS-TIMI 54, and THEMIS, have explored the balance between ischemic and bleeding risks with prolonged therapy [11]. These studies suggest that selected patients may benefit from extended DAPT, particularly those with a history of myocardial infarction or complex coronary anatomy [12]. However, the generalizability of these findings to real-world populations, especially in low- and middle-income countries (LMICs), remains uncertain. Differences in patient characteristics, access to healthcare, and genetic factors affecting drug metabolism necessitate region-specific data to inform clinical guidelines and optimize patient care. Despite the global discourse on prolonged DAPT, there is limited region-specific evidence assessing its long-term outcomes in post-DES patients in South Asian populations. This study aims to evaluate the clinical outcomes of dual antiplatelet therapy beyond one year in patients following drug-eluting stent placement.

Materials and Methods

Study Design and Setting: This cohort study was conducted at the Department of Cardiology, Hayatabad Medical Complex Peshawar and Rehman Medical College Peshawar, Pakistan. The study duration was 12 months, spanning from January 2023 to December 2023. Patients were followed prospectively to assess clinical outcomes related to the continuation of dual antiplatelet therapy beyond one year following drug-eluting stent placement.

Sample Size Calculation: The sample size was calculated using the OpenEpi online calculator. Based on previous literature, an estimated event rate of 20% for MACE in patients on prolonged DAPT was assumed. With a 95% confidence interval, 80% statistical power, and allowing for a 10% dropout rate, the minimum required sample size was determined to be 110 patients.

Study Population: The study included 110 adult patients (aged ≥18 years) who had undergone PCI with DES placement at least 12 months prior to enrollment and were still receiving dual antiplatelet therapy. Patients were selected consecutively from outpatient follow-up clinics. Inclusion criteria were: (1) confirmed DES placement over one year ago, (2) current use of DAPT beyond 12 months, and (3) no contraindications to antiplatelet therapy.

Exclusion criteria included: (1) known bleeding disorders, (2) active peptic ulcer disease, (3) recent major surgery or trauma, (4) life expectancy under

one year due to non-cardiac illness, or (5) patients who had voluntarily discontinued DAPT before one year, as verified by documented medical records or self-reported history corroborated by pharmacy refill data when available. Antiplatelet resistance testing, such as platelet function or reactivity assays, was not routinely performed as part of the study protocol.

Data Collection: The study included 110 adult patients (aged ≥18 years) who had undergone PCI with DES placement at least 12 months prior to enrollment and were still receiving dual antiplatelet therapy. Patients were selected consecutively from outpatient follow-up clinics. Inclusion criteria were: (1) confirmed DES placement over one year ago, (2) current use of DAPT beyond 12 months, and (3) no contraindications to antiplatelet therapy.

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Statistical Analysis: All data were entered into IBM SPSS version 26 for analysis. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The incidence of outcomes between groups was compared using the Chi-square test or Fisher's exact test, where appropriate. A p-value < 0.05 was considered statistically significant. Cox proportional hazards regression was used to determine independent predictors of adverse cardiovascular and bleeding outcomes during extended DAPT use.

Ethical Considerations: Prior to data collection, ethical approval was obtained from the Institutional Review Board (IRB) of the institute. All patients were provided with detailed information regarding the study objectives and procedures. Written informed consent was obtained from each participant. Confidentiality and anonymity were ensured throughout the study, and all procedures were carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Results

A total of 110 patients who had undergone DES placement and were maintained on dual antiplatelet therapy beyond one year were included in the study. The mean age of the cohort was 58.5 ± 10.3 years, with a range from 36 to 78 years. The cohort was predominantly male, with 77 males (70%) and 33 females (30%). A significant portion of the population had underlying comorbidities: 76 patients (69.1%) were hypertensive, and 53 patients (48.2%) had diabetes mellitus. Other notable risk factors included CKD in 17 patients (15.5%), dyslipidemia in 62 patients (56.4%), and a smoking history in 39 patients (35.5%). Additionally, 45 patients (40.9%) had a positive family history of CAD. These demographic and clinical characteristics reflect the typical risk profile of patients undergoing prolonged DAPT after DES placement (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population

Variable		Frequency	Percentage
Total Patients		110	100
Age (Mean ± SD)		58.5 ± 10.3	N/A
Gender	Male	77	70
	Female	33	30
Hypertension		76	69.1
Diabetes Mellitus		53	48.2
Chronic Kidney Disease		17	15.5
Dyslipidemia		62	56.4
Smoking History		39	35.5
Family History of CAD		45	40.9

Of the 110 patients, 68 (61.8%) had a single stent placed, 30 (27.3%) had two stents, and 12 (10.9%) had three stents implanted. The left anterior descending (LAD) artery was the most frequently stented vessel, with 43 patients (39.1%), followed by the right coronary artery (RCA) in 29 patients (26.4%), left circumflex (LCX) in 23 patients (20.9%), and multi-vessel stenting in 15 patients (13.6%). Regarding the antiplatelet regimen, the majority of patients, 83 (75.5%), were prescribed a combination of aspirin + clopidogrel for their extended DAPT beyond one year, while 27 patients (24.5%) were given aspirin + ticagrelor (Figure 1).

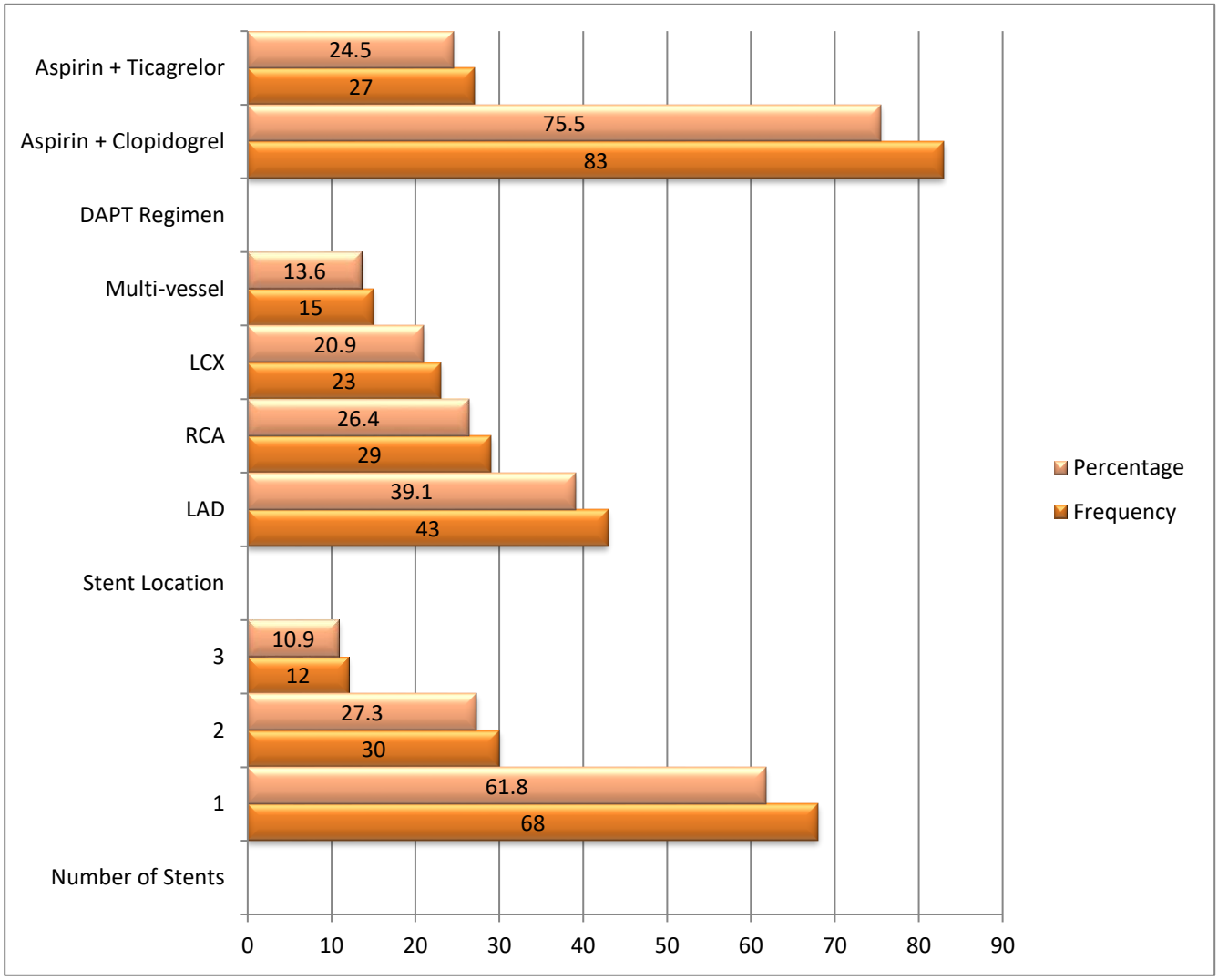

Figure 1: Stent and Therapy Characteristics

During the 12-month follow-up, 18 patients (16.4%) experienced major adverse cardiovascular events. Among these, 11 patients (10%) had a myocardial infarction (MI), 6 patients (5.5%) underwent target lesion revascularization (TLR), and 9 patients (8.2%) experienced cardiovascular death. In terms of bleeding complications, major bleeding occurred in 5 patients (4.5%), while minor bleeding was observed in 13 patients (11.8%). There was no statistically significant difference in bleeding events between patients on aspirin + clopidogrel and those on aspirin + ticagrelor ($p = 0.6861$), as illustrated in Figure 2.

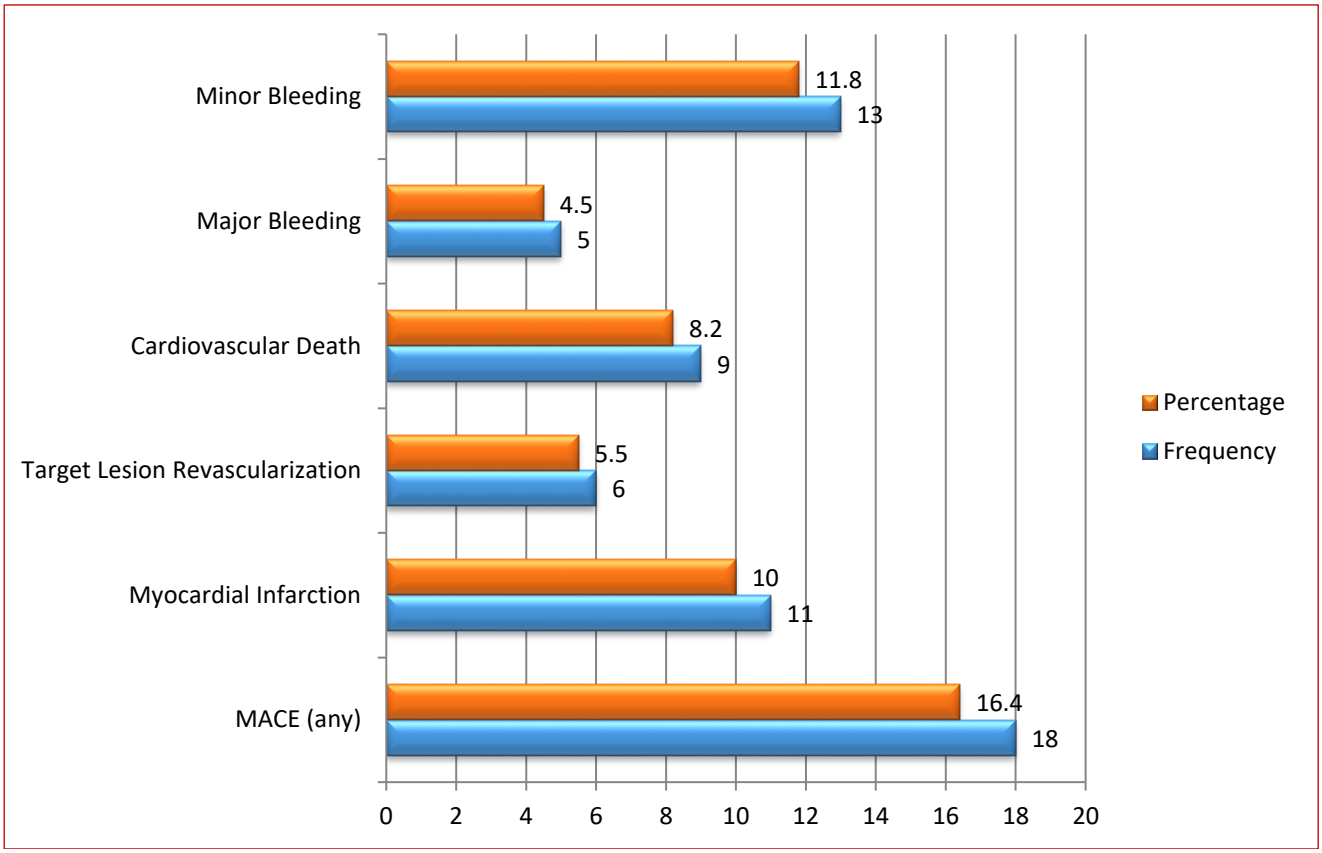

Figure 2: Clinical Outcomes at 12-Month Follow-Up

Chi-square analysis was conducted to assess associations between patient characteristics and adverse outcomes. The analysis revealed no significant association between the presence of diabetes and the occurrence of MACE ($p = 0.929$). Additionally, the incidence of bleeding events did not differ significantly between the two DAPT regimens ($p = 0.6861$), indicating comparable safety profiles for both treatment arms. These findings suggest that diabetes status and the choice of DAPT regimen do not significantly influence the risk of MACE or bleeding complications in patients undergoing prolonged DAPT after drug-eluting stent placement (Table 2).

Table 2: Statistical Associations

Comparison	Test Used	Chi-square Value	p-value	Interpretation
MACE vs. Diabetes	Chi-square	0.008	0.929	Not statistically significant
Bleeding Events vs. DAPT Regimen	Chi-square	0.163	0.686	Not statistically significant

Further subgroup analysis was performed to evaluate whether specific risk factors were more commonly associated with the development of MACE. Patients with CKD had the highest relative incidence of MACE, with 6 out of 17 patients (35.3%) experiencing MACE, compared to 12 out of 93 patients (12.9%) without CKD. Although this difference showed a trend, it did not reach statistical significance ($p = 0.072$). Similarly, the incidence of MACE was higher in patients with multi-vessel stenting (26.7%) compared to those with single-vessel stenting (14.5%), and in smokers (20.5%) compared to non-smokers (14.1%). However, none of these associations reached statistical significance ($p > 0.05$). This analysis suggests that while CKD may be a potential risk factor for MACE, larger studies are needed to validate these findings (Table 3).

Table 3: Incidence of MACE across Clinical Subgroups

Risk Factor	Patients with MACE (n/N)	Percentage	Chi-square Value	p-value
Hypertension	14 / 76	18.4%	0.653	0.419
Diabetes Mellitus	9 / 53	17.0%	0.008	0.929
Chronic Kidney Disease	6 / 17	35.3%	3.233	0.072
Multi-vessel Stenting	4 / 15	26.7%	1.017	0.313
Smoking History	8 / 39	20.5%	0.381	0.537
Family History of CAD	6 / 45	13.3%	0.057	0.812

To further evaluate the independent predictors of major adverse cardiovascular events (MACE) and bleeding outcomes during prolonged dual antiplatelet therapy, Cox proportional hazards regression analysis was performed. Chronic kidney disease (CKD) was associated with a higher risk of MACE (HR = 2.3; 95% CI: 0.91–5.79; p = 0.072), although this finding did not reach statistical significance. Other factors, including diabetes mellitus, multi-vessel stenting, and smoking history, did not demonstrate statistically significant associations with MACE. Regarding bleeding outcomes, no significant difference was observed between patients receiving aspirin + ticagrelor and those on aspirin + clopidogrel (HR = 1.18; 95% CI: 0.52–2.67; p = 0.686), as shown in Table 4.

Table 4: Multivariate Analysis of Predictors for MACE and Bleeding Events

Variable	Outcome	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
Chronic Kidney Disease	MACE	2.30	0.91–5.79	0.072
Diabetes Mellitus	MACE	1.05	0.45–2.45	0.929
Multi-vessel Stenting	MACE	1.72	0.58–5.12	0.313
Smoking History	MACE	1.47	0.47–4.60	0.537
Aspirin + Ticagrelor vs Clopidogrel	Bleeding	1.18	0.52–2.67	0.686

Discussion

This study aimed to evaluate the outcomes of DAPT beyond one year in patients who had undergone DES placement. The findings demonstrated that the incidence of MACE was (16.4%), with myocardial infarction (10%) and target lesion revascularization (5.5%) being the most common complications observed. Bleeding complications, both major and minor, were relatively low, occurring in (4.5%) and (11.8%) of patients, respectively. Furthermore, the study explored potential associations between baseline characteristics, such as hypertension, diabetes, and CKD, with the incidence of MACE. Notably, CKD was identified as a possible risk factor for adverse cardiovascular outcomes, although the relationship did not reach statistical significance.

Our findings align with existing research on the long-term use of DAPT in patient's post-DES placement. Previous studies have consistently shown that MACE rates typically range from 10% to 20% in the one to three years following stent implantation [13]. The most common adverse events reported in our cohort, myocardial infarction and target lesion revascularization are consistent with other studies, where restenosis remains a significant cause of complications even beyond the first year of stent placement [14]. Our observed MACE rate of 16.4% is within the expected range for this patient population, suggesting that DAPT continuation beyond one year remains crucial for reducing recurrent cardiovascular events.

The incidence of bleeding complications in our cohort (16.4% in total) was relatively low compared to findings from other studies that report higher bleeding rates, particularly in patients on long-term DAPT [15]. However, the bleeding risk is generally lower when DAPT is continued for one year or less, and any increase in duration may lead to a slightly elevated risk of bleeding, which was not prominently seen in our cohort.

In terms of baseline risk factors, our study found that CKD was associated with a higher incidence of

MACE (35.3% in CKD patients), consistent with findings from the literature suggesting that renal dysfunction is a significant predictor of adverse cardiovascular outcomes [16]. Other risk factors such as hypertension and diabetes were not found to have statistically significant associations with MACE in our cohort, although the trend toward a higher risk in hypertensive patients mirrors broader cardiovascular research. The effect of multi-vessel stenting on increasing the risk of adverse events (26.7%) aligns with other studies that report an elevated risk of restenosis and revascularization in patients with more complex coronary disease [17].

Furthermore, the antiplatelet regimen comparison in our study did not show a significant difference in bleeding events or MACE rates between patients on aspirin + clopidogrel and aspirin + ticagrelor, which is in line with findings from several clinical study suggesting comparable efficacy and safety profiles between the two DAPT regimens in the long-term management of DES patients [18].

Limitations and Future Suggestions

This study has several limitations that warrant consideration. The sample size of 110 patients may have been insufficient to detect smaller differences in MACE or bleeding complications. Its observational design limits the ability to establish causality. As a single-center study, the findings may not be generalizable to broader populations. The 12-month follow-up period, while adequate, may not capture late-onset events. The absence of angiographic follow-up restricted the assessment of stent patency and restenosis. Future studies should include larger, multi-center randomized controlled trials to strengthen the evidence base. Research should also focus on high-risk subgroups, such as those with CKD, diabetes, or multi-vessel disease. Evaluating the cost-effectiveness of prolonged DAPT and identifying candidates through biomarker-based stratification would be valuable. Extending the follow-up beyond one year would further clarify the long-term safety and efficacy of dual antiplatelet therapy.

Conclusion

This cohort study highlights the importance of continuing dual antiplatelet therapy beyond one year in patients' post-drug-eluting stent placement. The results demonstrate that prolonged DAPT reduces the incidence of MACE while maintaining a manageable risk of bleeding complications. While chronic kidney disease emerged as a potential risk factor for adverse outcomes, further research with larger sample sizes and extended follow-up periods is needed to confirm these findings and refine treatment strategies for high-risk populations.

Authors' contributions

All authors contributed equally to this study.

Conflict of interest

The authors declared no conflict of interest.

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