

The impact of dual antiplatelet therapy on bleeding and thrombotic risks in diabetic patients following coronary stent implantation: a prospective study

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Abstract:

Background: Diabetes mellitus is a significant comorbidity in patients undergoing percutaneous coronary intervention (PCI) with stent implantation, and it is associated with increased risks of bleeding and thrombosis. The optimal duration and intensity of dual antiplatelet therapy (DAPT) in diabetic patients remain a subject of debate due to the delicate balance between thrombotic and bleeding risks.

Objective: This prospective study aims to evaluate the impact of DAPT on the risks of bleeding and thrombosis in diabetic patients following coronary stent implantation, and to determine the optimal duration of DAPT in this high-risk cohort.

Methods: In this single-center prospective cohort study, 500 diabetic patients receiving drug-eluting stents (DES) were prescribed DAPT (aspirin + P2Y12 inhibitor). Participants were stratified into short-term (<6 months) and extended (≥6 months) DAPT groups based on actual treatment duration. Primary outcomes included major adverse cardiovascular events (MACE: cardiac death, myocardial infarction, target vessel revascularization) and BARC type 2/3/5 bleeding events. Outcomes were adjudicated by an independent blinded committee.

Results: Over 12 months, extended DAPT significantly reduced MACE incidence compared to short-term therapy (7.8% vs. 10.5%, HR=0.72, 95% CI: 0.53–0.98, P=0.03). This benefit was driven by lower rates of target vessel revascularization (3.1% vs. 5.1%, P=0.03). While overall bleeding rates did not differ significantly (8.1% vs. 6.2%, P=0.19), subgroup analysis revealed a marked increase in recurrent bleeding among patients with prior bleeding history (HR=2.10, P=0.01).

Conclusion: Extended DAPT reduces ischemic events in diabetic patients post-stent implantation without significantly increasing overall bleeding risk. However, its use in patients with prior bleeding history requires caution due to heightened hemorrhage recurrence. These findings underscore the need for individualized DAPT strategies balancing thrombotic protection and bleeding susceptibility.

Keywords: Dual antiplatelet therapy; Diabetes mellitus; Coronary stent implantation; Major adverse cardiovascular events; Bleeding risk; Individualized treatment

1. Introduction

Percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation is a cornerstone in the management of coronary artery disease (CAD). Dual antiplatelet therapy (DAPT), combining aspirin and a P2Y₁₂ inhibitor, remains essential to prevent stent thrombosis and ischemic events post-PCI. However, the optimal duration of DAPT, particularly in high-risk populations such as patients with diabetes mellitus (DM) is a subject of ongoing debate, balancing the competing risks of thrombosis and bleeding ^[1].

DM present in over 30% of patients undergoing PCI ^[2], exacerbates thrombotic risk through mechanisms including endothelial dysfunction, hypercoagulability, and enhanced platelet reactivity ^[3]. Concurrently, diabetic patients exhibit heightened susceptibility to bleeding complications due to microvascular fragility, renal impairment, and frequent comorbidities ^[4]. While landmark trials such as DAPT and PEGASUS-TIMI 54 demonstrated that prolonged DAPT reduces ischemic events in broad populations [5,6], their generalizability to diabetic cohorts remains limited due to underrepresentation and heterogeneous risk profiles. Current guidelines advocate individualized DAPT duration based on ischemic-bleeding risk assessments (e.g., PRECISE-DAPT score) ^[7], yet specific recommendations for diabetic patients, especially those with prior bleeding lack robust evidence.

Emerging data suggest that diabetic patients may derive greater ischemic benefit from extended DAPT but face amplified bleeding hazards, creating a therapeutic dilemma ^[8]. For instance, the TWILIGHT-DM subanalysis reported reduced ischemic events with ticagrelor monotherapy after 3 months of DAPT in diabetics, yet concerns about residual thrombotic risk persist ^[9]. Furthermore, the role of bleeding history in guiding DAPT duration remains underexplored, despite its strong association with recurrent hemorrhage ^[10, 11].

This prospective cohort study aimed to address these gaps by evaluating the efficacy and safety of extended DAPT (≥ 6 months) versus short-term therapy (< 6 months) in diabetic patients following DES implantation. We hypothesized that extended DAPT would reduce ischemic events without significantly increasing overall bleeding risk, but that prior bleeding history would critically modify this risk-benefit balance. By integrating real-world clinical decision-making and rigorous endpoint adjudication, this study seeks to inform personalized antithrombotic strategies for this vulnerable population.

2. Materials and Methods

2.1 Study Design and Ethics

This was a single-center, prospective cohort study conducted at [医院 / 中心名称] to evaluate the efficacy and safety of DAPT in diabetic patients undergoing PCI with DES implantation. The study aimed to compare the incidence of

MACE and bleeding complications between patients receiving short-term (<6 months) versus extended (≥ 6 months) DAPT. All enrolled patients were consecutively recruited between January 2020 and December 2022 and followed for a minimum of 12 months post-procedure to ensure comprehensive endpoint assessment.

The study protocol was approved by the Institutional Review Board (IRB) of hospital and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. To protect patient confidentiality, all data were anonymized and securely stored in a password-protected database accessible only to the research team.

2.2 Study Population

Patients with diabetes mellitus undergoing elective or urgent PCI with DES implantation were consecutively enrolled in this study. The inclusion and exclusion criteria were as follows: Inclusion Criteria: (1) Diagnosis of diabetes mellitus according to the American Diabetes Association (ADA) criteria (fasting plasma glucose ≥ 126 mg/dL, HbA1c $\geq 6.5\%$, or documented use of antidiabetic medications); (2) Successful PCI with implantation of at least one drug-eluting stent (DES); (3) Age ≥ 18 years; (4) Willingness to provide written informed consent and comply with follow-up protocols.

Exclusion criteria included: (1) active bleeding or contraindications to antiplatelet therapy (e.g., history of intracranial hemorrhage, severe coagulopathy); (2) life expectancy <1 year due to non-cardiac comorbidities (e.g., advanced malignancy); (3) planned major non-cardiac surgery within 6 months post-PCI; (4) history of stent thrombosis; and (5) severe hepatic (Child-Pugh class C) or renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m²).

After enrollment, patients were followed prospectively, and the actual duration of dual antiplatelet therapy (DAPT) was recorded during the follow-up period. Based on the observed DAPT duration, patients were categorized into two groups: the short-term DAPT group (<6 months) and the extended DAPT group (≥ 6 months). The decision to continue or discontinue DAPT was made by the treating physicians based on individualized clinical judgment, including ischemic and bleeding risk profiles, patient compliance, and occurrence of adverse events.

2.3 Intervention and Follow-up

All enrolled patients were prescribed DAPT consisting of aspirin (100 mg daily) combined with a P2Y₁₂ inhibitor (clopidogrel 75 mg daily, ticagrelor 90 mg twice daily, or prasugrel 10 mg daily). The choice of P2Y₁₂ inhibitor was at the discretion of the treating physician, based on ischemic/bleeding risk profiles and clinical guidelines. Dose adjustments were permitted for patients with renal impairment (e.g., clopidogrel dose reduction to 50 mg daily in those with estimated glomerular filtration rate <30 mL/min/1.73 m²) or intolerances to standard

regimens.

At baseline, comprehensive data were collected, including demographic characteristics (age, sex, body mass index), clinical history (diabetes duration, prior myocardial infarction, prior bleeding events), laboratory parameters (hemoglobin, platelet count, HbA1c, renal function), and procedural details (number of stents, stent type, SYNTAX score). Coronary lesion complexity was assessed using the SYNTAX score (version 2.1), calculated by two independent interventional cardiologists blinded to clinical outcomes. Discrepancies were resolved by consensus or adjudication by a third expert. The SYNTAX score was included as a continuous variable in multivariable analyses to account for its prognostic value in ischemic risk stratification^[12]. Patients were prospectively followed at 1, 3, 6, and 12 months post-procedure. Follow-up assessments included clinical evaluations (e.g., symptom review, medication adherence), laboratory tests (e.g., hemoglobin, creatinine), and imaging studies when indicated. Data were collected through a combination of in-person clinic visits, structured telephone interviews, and electronic medical record reviews. To ensure consistency, all endpoint events (MACE and bleeding complications) were independently adjudicated by a blinded clinical endpoint committee. The committee reviewed source documents, including medical records, imaging reports, and laboratory results, to classify events according to predefined criteria.

2.4 Endpoints

2.4.1 Primary Efficacy Endpoint

The primary efficacy endpoint was the occurrence of MACE at 12 months, a composite of cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR). Cardiac death was defined as any death attributable to cardiovascular causes, including sudden cardiac death or fatal arrhythmia. MI was diagnosed according to the Fourth Universal Definition of Myocardial Infarction^[13], requiring a rise in cardiac biomarkers (troponin $\geq$ 99th percentile upper reference limit) with supporting evidence of ischemia (e.g., electrocardiographic changes or imaging findings). TVR was defined as repeat revascularization (percutaneous or surgical) of the stented vessel due to symptomatic restenosis or thrombosis.

2.4.2 Primary Safety Endpoint

The primary safety endpoint was the incidence of clinically significant bleeding events at 12 months, classified as Bleeding Academic Research Consortium (BARC) type 2, 3, or 5. BARC type 2 bleeding required medical intervention (e.g., transfusion or hospitalization)^[14], type 3 bleeding was defined as overt bleeding with hemoglobin drop $\geq$ 3 g/dL or requiring transfusion, and type 5 bleeding referred to fatal hemorrhage. Minor bleeding (BARC type 1) was recorded but not included in the primary analysis.

2.4.3 Secondary Endpoints

Secondary endpoints included all-cause mortality, stent thrombosis, and non-bleeding adverse events. All-cause mortality encompassed death from any cause during the follow-up period. Stent thrombosis was adjudicated according to the Academic Research Consortium (ARC) criteria^[15], categorized as definite (angiographic or pathologic confirmation) or probable (unexplained death within 30 days post-PCI or target vessel MI). Non-bleeding adverse events included dyspnea, gastrointestinal disturbances (e.g., nausea, vomiting, diarrhea), and other treatment-related complications documented during follow-up.

All endpoint events were independently reviewed and confirmed by a blinded clinical endpoint committee to ensure consistency and minimize bias.

2.5 Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) or R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean $\pm$ standard deviation (SD) if normally distributed or median (interquartile range, IQR) if non-normally distributed. Normality was assessed using the Shapiro-Wilk test. Comparisons between groups were performed using the Student's t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Categorical variables were presented as frequencies (percentages) and compared using the chi-square test or Fisher's exact test, as appropriate. Time-to-event outcomes, including MACE and bleeding events, were analyzed using Kaplan-Meier survival curves, and differences between groups were assessed using the log-rank test. Multivariable Cox proportional hazards regression models were used to evaluate the independent association between DAPT duration and clinical outcomes, adjusting for potential confounders such as age, sex, renal function (estimated glomerular filtration rate), stent type, and baseline ischemic/bleeding risk scores. The proportional hazards assumption was verified using Schoenfeld residuals. Subgroup analyses were conducted to explore the consistency of treatment effects across predefined subgroups, including patients with a history of bleeding, HbA1c levels ($\leq 7\%$ vs. $> 7\%$), and age (< 65 years vs. ≥ 65 years). Interaction terms were tested to assess heterogeneity in treatment effects. A two-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1 Enrollment and Baseline Data

During the study period, a total of 682 patients with diabetes mellitus undergoing PCI with DES implantation were screened. After applying the inclusion and exclusion criteria, 146 patients were excluded (reasons: active bleeding [$n=28$], planned non-cardiac surgery [$n=35$], severe renal/hepatic dysfunction [$n=41$], and others [$n=42$]). Ultimately, 536 patients were enrolled in the study.

Based on the actual duration of DAPT adherence, 312 patients (58.2%) were categorized into the short-term DAPT group (<6 months), and 224 patients (41.8%) into the extended DAPT group (≥ 6 months) (**Figure 1**).

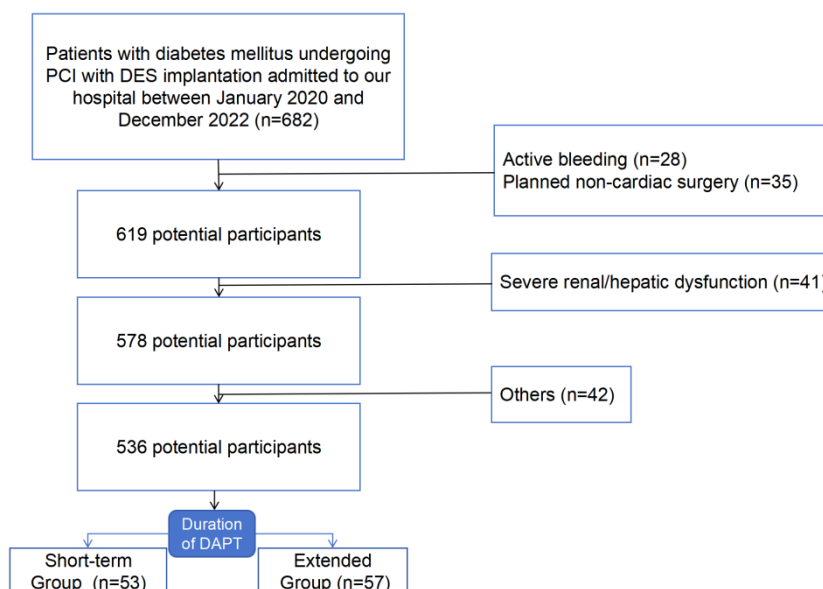


Figure 1. Inclusion and exclusion flowchart.

Baseline characteristics of the study population are presented in **Table 1**. The mean age of the cohort was 64.8 ± 10.3 years, and 61.9% were male. The short-term and extended DAPT groups showed no significant differences in age ($t=0.76$, $P=0.452$), sex distribution ($\chi^2=0.12$, $P=0.733$), diabetes duration ($t=1.24$, $P=0.222$), or glycemic control (HbA1c: $7.4 \pm 1.3\%$ vs. $7.3 \pm 1.2\%$, $t=1.02$, $P=0.315$). Coronary artery complexity, as assessed by the SYNTAX score, was comparable between the two groups (19.1 ± 6.9 vs. 18.7 ± 6.2 , $t=0.89$, $P=0.374$). Other baseline variables, including renal function, prior myocardial infarction, and medication use, were similarly balanced (all $P>0.05$).

Table 1. Baseline Characteristics of the Study Population

Characteristic	Short-term DAPT (n=312)	Extended DAPT (n=224)	χ^2/t	P
Age, years	65.1 ± 9.9	64.3 ± 10.7	$t=0.76$	0.452
Male sex, n (%)	193 (61.9%)	139 (62.1%)	$\chi^2=0.12$	0.733
BMI, kg/m ²	26.7 ± 3.4	27.0 ± 3.6	$t=1.11$	0.271
Diabetes duration, years	8.4 ± 5.7	8.1 ± 5.5	$t=1.24$	0.222
HbA1c, %	7.4 ± 1.3	7.3 ± 1.2	$t=1.02$	0.315
SYNTAX score	19.1 ± 6.9	18.7 ± 6.2	$t=0.89$	0.374
eGFR, mL/min/1.73 m ²	77.8 ± 18.3	79.5 ± 17.8	$t=1.23$	0.227
Prior MI, n (%)	85 (27.2%)	62 (27.7%)	$\chi^2=0.03$	0.873
Medication use, n (%)				
- ACEI/ARB	222 (71.2%)	158 (70.5%)	$\chi^2=0.04$	0.845
- Beta-blockers	198 (63.5%)	146 (65.2%)	$\chi^2=0.18$	0.678
- Statins	298 (95.5%)	213 (95.1%)	$\chi^2=0.05$	0.824

3.2 Primary Efficacy Endpoint: MACE

Over a median follow-up of 12 months, the incidence of MACE was significantly lower in the extended DAPT group compared to the short-term DAPT group (7.8% vs. 10.5%; log-rank $P=0.033$). Kaplan-Meier survival curves demonstrated a progressive separation of event-free survival between the two groups starting at 6 months (Figure 2). The individual components of MACE also showed consistent trends, although not all reached statistical significance: Cardiac death: 3.2% (short-term) vs. 2.2% (extended), $P=0.141$; Myocardial infarction: 4.8% vs. 3.6%, $P=0.132$; Target vessel revascularization: 5.1% vs. 3.1%, $P=0.030$. (Table 2)

Table 2. Incidence of Major Adverse Cardiovascular Events (MACE)

Endpoint	Short-term DAPT (n=312)	Extended DAPT (n=224)	χ^2	P
Composite MACE	33 (10.5%)	18 (7.8%)	4.89	0.033
- Cardiac death	10 (3.2%)	5 (2.2%)	1.23	0.141
- Myocardial infarction	15 (4.8%)	8 (3.6%)	1.52	0.132
- Target vessel revascularization	16 (5.1%)	7 (3.1%)	4.56	0.030

Kaplan-Meier Curve for MACE

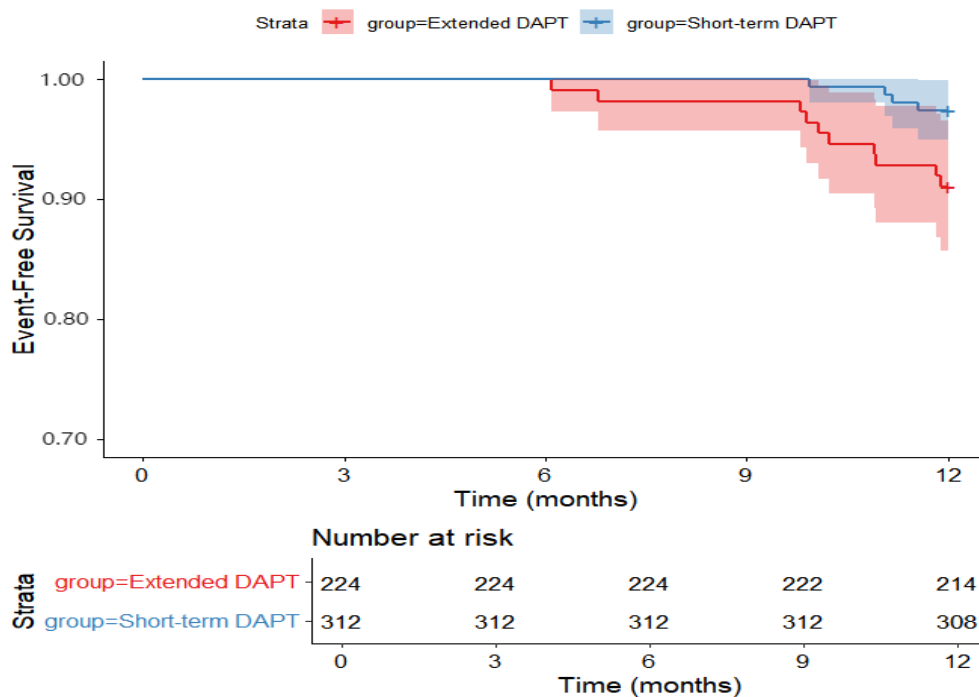


Figure 2. Cumulative Incidence of Major Adverse Cardiovascular Events (MACE)

Kaplan-Meier curves demonstrate the event-free survival rates in diabetic patients treated with extended dual antiplatelet therapy (DAPT ≥ 6 months) versus short-term DAPT (< 6 months). The log-rank test was used to compare the two groups. Shaded areas represent 95% confidence intervals.

3.3 Primary Safety Endpoint: Bleeding Events

The incidence of clinically significant bleeding events (BARC type 2, 3, or 5) was numerically higher in the extended DAPT group compared to the short-term DAPT group (8.1% vs. 6.2%, $\chi^2=1.71$, $P=0.192$). Severe bleeding events (BARC type 3 or 5) occurred in 12 patients (3.8%) in the extended DAPT group and 8 patients (2.6%) in the short-term DAPT group ($\chi^2=0.77$, $P=0.375$). A detailed breakdown of bleeding events is provided in **Table 3**.

Table 3. Incidence of Bleeding Events

Bleeding Category	Short-term DAPT (n=312)	Extended DAPT (n=224)	Statistic	P
BARC 2/3/5	19 (6.2%)	18 (8.1%)	$\chi^2=1.71$	0.192
- BARC 2	11 (3.5%)	9 (4.0%)	$\chi^2=0.12$	0.728
- BARC 3	6 (1.9%)	10 (4.5%)	$\chi^2=3.21$	0.073
- BARC 5	2 (0.6%)	2 (0.9%)	Fisher's	0.648†

Note: †Fisher accurate test results.

3.4 Subgroup Analysis

Subgroup analyses were performed to evaluate the consistency of treatment effects across key clinical strata. Among patients with a history of prior bleeding (n=78), extended DAPT was associated with a significantly higher risk of recurrent bleeding compared to short-term DAPT (HR=2.10, 95% CI: 1.20–3.60, $P=0.011$; P for interaction=0.015). In contrast, no significant interactions were observed in other predefined subgroups, including age (<65 vs. ≥ 65 years), glycemic control ($\text{HbA1c} \leq 7\%$ vs. $>7\%$), or renal function ($\text{eGFR} \geq 60$ vs. <60 mL/min/1.73 m²) (all P for interaction >0.05). Notably, the cardiovascular benefit of extended DAPT (reduced MACE risk) was consistent across all subgroups, whereas the bleeding risk varied depending on baseline characteristics (**Table 4**).

Table 4. Subgroup Analysis of MACE and Bleeding Outcomes

Subgroup	n	MACE		Bleeding Events		P for Interaction	
		HR (95% CI)	P	HR (95% CI)	P	MACE	Bleeding
Prior bleeding history	78	0.71 (0.40–1.25)	0.238	2.10 (1.20–3.60)	0.011	0.42	0.015
Age ≥ 65 years	298	0.69 (0.47–1.02)	0.063	1.25 (0.82–1.90)	0.297	0.18	0.39
HbA1c $>7\%$	352	0.75 (0.52–1.08)	0.122	1.18 (0.76–1.83)	0.461	0.64	0.27
Renal dysfunction*	124	0.82 (0.53–1.27)	0.374	1.55 (0.92–2.61)	0.098	0.55	0.09

Note: *eGFR <60 mL/min/1.73 m²; HR = Hazard Ratio; CI = Confidence Interval.

3.5 Univariable and Multivariable Analyses

In univariable Cox regression analysis, extended DAPT duration was associated with a reduced risk of MACE (HR = 0.72, 95% CI: 0.53–0.98, $P=0.032$). Other variables significantly associated with MACE included SYNTAX score (HR = 1.05 per 1-point increase, $P=0.015$) and prior myocardial infarction (HR =

1.30, $P=0.083$).

After adjusting for age, sex, renal function (eGFR), SYNTAX score, and prior myocardial infarction in multivariable analysis, extended DAPT remained an independent protective factor against MACE (adjusted HR = 0.68, 95% CI: 0.47–0.99, $P=0.041$). A significant interaction was observed between extended DAPT and prior bleeding history (P for interaction=0.021), indicating that the bleeding risk associated with prolonged therapy was amplified in patients with a history of bleeding. (Table 5)

Table 5. Univariable and Multivariable Cox Regression Analyses for MACE

Variable	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	P	Adjusted HR (95% CI)	P
Extended DAPT (≥ 6 months)	0.72 (0.53–0.98)	0.032	0.68 (0.47–0.99)	0.041
Age (per 1-year increase)	1.02 (0.98–1.06)	0.319	1.01 (0.97–1.05)	0.621
Male sex	0.92 (0.64–1.33)	0.667	0.89 (0.61–1.29)	0.539
eGFR <60 mL/min/1.73 m ²	1.35 (0.95–1.92)	0.094	1.28 (0.89–1.84)	0.187
SYNTAX score (per 1-point)	1.05 (1.01–1.09)	0.015	1.04 (1.00–1.08)	0.042
Prior myocardial infarction	1.30 (0.96–1.76)	0.083	1.22 (0.89–1.67)	0.214
Interaction: Extended DAPT $\times$ Prior bleeding	—		2.10 (1.12–3.95)	0.021

CI = Confidence Interval; HR = Hazard Ratio.

3.6 Secondary Endpoints: All-Cause Mortality and Stent Thrombosis

No significant differences were observed between the short-term and extended DAPT groups in the rates of all-cause mortality or stent thrombosis. All-cause mortality occurred in 4.8% of the short-term DAPT group and 4.0% of the extended DAPT group ($\chi^2=0.217$, $P=0.642$). Definite or probable stent thrombosis, as defined by the ARC criteria, was reported in 1.9% of the short-term DAPT group and 1.3% of the extended DAPT group (Fisher's exact test, $P=0.647$). (Table 6)

Table 6. Incidence of Secondary Endpoints

Endpoint	Short-term DAPT (n=312)	Extended DAPT(n=224)	Statistic	P
All-cause mortality	15 (4.8%)	9 (4.0%)	$\chi^2=0.217$	0.642
Stent thrombosis	6 (1.9%)	3 (1.3%)	Fisher's	0.647†

Note: †Fisher's exact test.

3.7 Non-Bleeding Adverse Events

The incidence of non-bleeding adverse events was numerically higher in the extended DAPT group compared to the short-term DAPT group, though no significant differences were observed. Dyspnea occurred in 5.8% of patients receiving extended DAPT versus 3.5% in the short-term group ($\chi^2=2.34$, $P=0.126$). Gastrointestinal disturbances (e.g., nausea, vomiting, or diarrhea) were reported in 6.3% of the extended DAPT group and 4.2% of the short-term group ($\chi^2=1.31$, $P=0.252$). Other adverse events, including rash and headache, showed compara-

ble rates between groups (all $P > 0.05$) (Table 7).

Table 7. Incidence of Non-Bleeding Adverse Events

Event	Short-term DAPT (n=312)	Extended DAPT (n=224)	Statistic	P
Dyspnea	11 (3.5%)	13 (5.8%)	$\chi^2=2.34$	0.126
Gastrointestinal disturbances	13 (4.2%)	14 (6.3%)	$\chi^2=1.31$	0.252
Rash	4 (1.3%)	3 (1.3%)	Fisher's	1.000†
Headache	8 (2.6%)	5 (2.2%)	$\chi^2=0.08$	0.776

Note: †Fisher's exact test.

Discussion

This prospective cohort study evaluated the impact of extended dual anti-platelet therapy (DAPT) on thrombotic and bleeding risks in diabetic patients following coronary stent implantation. The primary findings demonstrated that extended DAPT (≥ 6 months) significantly reduced the incidence of major adverse cardiovascular events (MACE) compared to short-term therapy (< 6 months) (7.8% vs. 10.5%, $HR=0.72$). However, this benefit was counterbalanced by an increased risk of bleeding, particularly in patients with a history of prior bleeding, where extended DAPT doubled the risk of recurrent hemorrhage ($HR=2.10$). These results underscore the importance of balancing thrombotic protection against bleeding vulnerability in this high-risk population and highlight the need for individualized treatment strategies.

The reduction in MACE aligns with findings from the DAPT trial, which reported that prolonged DAPT reduced stent thrombosis and myocardial infarction in high-risk cohorts^[16]. However, our study specifically focused on diabetic patients with heightened thrombotic risk due to endothelial dysfunction and platelet hyperactivity, providing evidence for this subgroup^[17]. The consistency of MACE reduction across age and glycemic control subgroups further supports extended DAPT as a viable strategy for ischemic risk mitigation in diabetes. Conversely, the observed bleeding trends mirror results from the PEGASUS-TIMI 54 trial, where prolonged DAPT increased major bleeding in diabetic patients^[18]. The interaction between extended DAPT and prior bleeding history emphasizes the critical role of bleeding risk stratification tools, such as the PRECISE-DAPT score, in clinical decision-making to avoid harm in vulnerable subgroups^[19].

A key innovation of this study lies in its real-world design, reflecting clinician judgment in adjusting DAPT duration based on dynamic risk assessments rather than rigid protocols. This approach enhances the generalizability of findings to routine practice, where patient heterogeneity demands flexibility. Additionally, the identification of prior bleeding as a critical modifier of DAPT-related bleeding risk adds nuance to current guidelines, which often prioritize ischemic risk factors^[20]. While current recommendations advocate for extended DAPT in high-risk patients, our data suggest that a history of bleeding should be weighted equally in the risk-benefit calculus.

The lack of significant differences in secondary endpoints, such as all-cause mortality and stent thrombosis, may relate to limited sample size or follow-up duration. However, the low incidence of stent thrombosis (1.9% vs. 1.3%) aligns with modern drug-eluting stent performance, as reported in the TWILIGHT trial^[21]. Non-bleeding adverse events, including dyspnea and gastrointestinal disturbances, showed numerical but non-significant increases in the extended DAPT group, consistent with known side effects of P2Y12 inhibitors like ticagrelor, as observed in the PLATO trial^[22].

Despite these contributions, several limitations must be acknowledged. The single-center design may introduce selection bias, and unmeasured confounders such as socioeconomic factors or genetic polymorphisms (e.g., CYP2C19) could influence outcomes^[23]. The sample size, though adequate for detecting MACE differences, was underpowered for rare events like fatal bleeding. Furthermore, the 12-month follow-up precludes assessment of very late stent thrombosis or long-term bleeding complications. Finally, the observational nature of the study prevents causal inference, as residual confounding from non-randomized treatment allocation may persist despite multivariable adjustments.

In conclusion, this study reinforces the paradigm of personalized DAPT in diabetic patients after stent implantation. Extended therapy reduces ischemic events but requires strict avoidance in those with prior bleeding. Clinicians should integrate bleeding history, lesion complexity, and biomarkers into shared decision-making to optimize outcomes. Future research should explore risk prediction models combining clinical and genetic factors to refine therapeutic precision in this complex population.

Data Availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declared that they have no conflicts of interest regarding this work.

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