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Impact of pre-stenting antiplatelet therapy regimens on clinical outcomes following carotid artery stenting: a retrospective analysis

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ABSTRACT

Objectives: This study investigates the influence of various antiplatelet regimens before carotid artery stenting (CAS) on short-term and long-term clinical outcomes. Effective antiplatelet therapy is vital for enhancing the success and safety of CAS. Determining the best approach remains a priority.

Methods: This retrospective cohort analysis involved 235 patients who underwent CAS at a single institution between October 2020 and October 2024. Participants were divided into three groups based on the antiplatelet regimen administered before the procedure: dual antiplatelet therapy (DAPT), aspirin monotherapy (SAPT-A), and clopidogrel monotherapy (SAPT-C). The main outcomes evaluated were stroke, transient ischemic attack (TIA), and bleeding complications. Secondary outcomes included restenosis, stent thrombosis, and death. Statistical methods were applied to compare outcomes across the groups.

Results: Stroke (0.8%) and TIA (2.5%) were notably less frequent in the DAPT group compared to the SAPT-A (7.1% and 12.5%, respectively) and SAPT-C (6.9% and 8.6%, respectively) groups ($P<0.05$). Rates of stent thrombosis (1.7%-1.8%) and mortality (0.8%-3.4%) at six months showed no significant differences among the groups ($P>0.05$).

Conclusions: Pre-procedural DAPT reduces short-term ischemic complications in CAS. However, long-term outcomes were comparable across regimens. These findings suggest that antiplatelet strategies should be individualized. Larger studies with longer follow-ups are needed.

Keywords: Carotid artery stenting, dual antiplatelet therapy, aspirin, clopidogrel, ischemic complications, restenosis, transient ischemic attack

Carotid artery stenosis is a major risk factor for ischemic stroke, significantly contributing to cerebrovascular morbidity and mortality [1]. The annual risk of stroke in asymptomatic individuals with ≥50% carotid artery stenosis ranges from less than 1% to approximately 4.3% [2-5]. Carotid artery stenting (CAS) was introduced in the early 1990s as a less invasive option for revascularization, particularly suited for patients at high surgical risk or with challenging anatomical considerations[6, 7]. Although CAS has demonstrated efficacy and an acceptable safety profile, ischemic complications due to distal

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embolization and atherothrombosis still pose significant challenges, requiring optimization of pre- and post-procedural management strategies. Antiplatelet therapy plays a critical role in CAS by reducing the risk of thrombotic events. Aspirin is still a key antithrombotic agent, but its variable efficacy among patients has highlighted the complementary benefits of Adenosine diphosphate (ADP) receptor antagonists such as clopidogrel and ticlopidine, which have shown improved outcomes when combined with aspirin in stent procedures [8, 9]. Studies have specifically demonstrated that dual antiplatelet therapy with clopidogrel and aspirin effectively reduces complications following CAS [10-12]. Dual antiplatelet therapy with clopidogrel and aspirin has been linked to a low rate of ischemic complications after CAS. Additionally, clopidogrel has shown superior efficacy compared to ticlopidine [13]. In a study investigating late stent thrombosis due to delayed endothelialization for the importance of long-term antiplatelet therapy, early discontinuation of antiplatelet therapy within the first 9 months after the procedure in patients with drug-eluting stents emerged as an important risk factor [14]. CAS is a minimally invasive option for revascularization in high-risk surgical patients, and additional antiplatelet therapy is crucial to manage ischemic complications, reduce distal embolization and prevent both early and late atherothrombotic events, thus improving the long-term success of the procedure [15].

With the growing use of CAS, understanding the influence of various antiplatelet regimens on procedural and long-term outcomes is crucial. This study aimed to assess the effects of pre-procedural antiplatelet therapy on ischemic and hemorrhagic outcomes in patients undergoing CAS and to offer insights for optimizing treatment strategies to enhance procedural safety and efficacy.

METHODS

Study Design and Population

This study was conducted at a tertiary hospital between October 2020 and October 2024. It adhered to the 2008 Declaration of Helsinki and was approved by the Clinical Research Ethics Committee (Approval No: 2024/22-1). Patient data were anonymized to maintain confidentiality.

The inclusion criteria encompassed patients aged 18 years or older with significant carotid artery stenosis, defined as ≥50% stenosis for symptomatic patients and ≥70% for asymptomatic patients. The diagnosis was confirmed using imaging modalities, including Doppler ultrasound, CT angiography, or MR angiography, which were used primarily to assess the degree of stenosis. Plaque composition and morphology were not routinely evaluated in this study. However, restenosis and stent thrombosis were assessed using follow-up imaging. Comprehensive medical records documenting clinical, procedural, and follow-up data at 24 hours, 1 month, and 6 months postoperatively were mandatory.

A total of 312 carotid artery stenting (CAS) procedures were performed at our institution between October 2020 and October 2024. After applying the study's inclusion and exclusion criteria, 77 patients were excluded for the following reasons:

•Previous carotid intervention (n=21) (stenting or endarterectomy)

•Non-atherosclerotic carotid stenosis (n=18) (e.g., arterial dissection, vasculitis)

•Contraindications to antiplatelet therapy (n=13) (e.g., active bleeding, severe allergic reactions)

•Incomplete medical records (n=15) (e.g., missing procedural or follow-up data)

•Non-adherence to pre- or post-procedural antiplatelet therapy (n=10)

•After these exclusions, 235 patients were included in the final analysis.

Procedure Details

CAS was performed under local anesthesia with mild sedation to enable patient feedback during the procedure. Access was achieved via the femoral artery, and a guiding catheter was advanced to the stenotic segment of the carotid artery. A distal embolic protection device was used to reduce the risk of embolization. Balloon angioplasty was employed for pre-dilatation of the stenosis, followed by the deployment of a self-expanding stent to maintain vessel patency. Upon stent placement, the embolic protection device was retrieved, and completion angiography was performed to confirm successful revascularization. Postoperative follow-up included regular assessments, with specific evaluations of headache conducted as per the study's follow-up protocol.

CAS was performed by experts with extensive experience and adhered to standardized institutional protocols to maintain consistency across cases.

Antiplatelet Therapy

Patients were categorized into three groups based on their antiplatelet regimen prior to carotid artery stenting: (1) Dual Antiplatelet Therapy (DAPT): Combination of clopidogrel and aspirin; (2) Single Antiplatelet Therapy - Aspirin (SAPT-A): Aspirin alone; and (3) Single Antiplatelet Therapy - Clopidogrel (SAPT-C): Clopidogrel alone.

As this is a retrospective study, the allocation to antiplatelet regimens was determined by treating physicians at the time of care, based on clinical judgment and patient-specific factors. Eligibility criteria required patients to have been on antiplatelet therapy for at least one month before the procedure to ensure sufficient platelet inhibition. After CAS, all patients were prescribed dual antiplatelet therapy (DAPT) with aspirin and clopidogrel for six months to minimize the risk of ischemic events and stent thrombosis. Following this period, the regimen was transitioned to aspirin monotherapy for long-term secondary stroke prevention. Compliance with the antiplatelet regimen was monitored during follow-up visits at one and six months.

Outcome Measures

The primary outcomes were the incidence of ischemic events, including stroke and transient ischemic attacks (TIA), and hemorrhagic complications, such as intracranial and extracranial bleeding, within 30 days and during the 6-month follow-up. Secondary outcomes included stent thrombosis, restenosis identified through follow-up imaging, and all-cause mortality at 6 months. Procedural success was defined as achieving residual stenosis of <30% without peri-procedural complications.

Data Collection

Demographic, clinical, and procedural data were systematically retrieved from electronic medical records. Collected variables included patient age, gender, comorbidities (e.g., hypertension, diabetes mellitus, and coronary artery disease), stenosis grade, pre-procedural antiplatelet regimen, and procedural details. Follow-up data were collected at 24 hours, 1 month, and 6 months post-procedure. These included imaging findings to evaluate restenosis, detailed records of is-

Table 1. Distribution of demographic data of patients according to antiplatelet use

Variables		Anticoagulant usage			
		DAPT (n=121)	SAPT-A (n=56)	SAPT-C (n=58)	P value
Gender	Male	89	40	35	0.188†
	Female	32	16	23	
Hypertension	No	19	10	18	0.051†
	Yes	102	46	40	
Diabetes mellitus	No	60	26	32	0.634†
	Yes	61	30	26	
Symptomatic stenosis	No	46	21	27	0.501†
	Yes	75	35	31	
			Mean±SD		
Age		62.3±2.8	62.7±2.8	63.2±3.2	0.151‡
Stenosis degree (%)		77.5±6	74.0±7.2	75.2±7.1	0.069‡

DAPT=Dual Antiplatelet Therapy, SAPT-A=Single Antiplatelet Therapy-Aspirin, SAPT-C=Single Antiplatelet Therapy-Clopidogrel, SD=standard deviation

†Chi-Square Test, ‡One Way ANOVA Test

chemic and hemorrhagic events, and adherence to prescribed antiplatelet therapy.

Statistical Analysis

Statistical analyses were conducted using IBM® SPSS® Statistics version 25 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to evaluate the normality of numerical data. Qualitative variables were expressed as frequencies and percentages, while continuous variables were presented as mean±standard deviation. Categorical variables were compared using the Chi-square test, and relationships between numerical variables and anticoagulant treatment groups were analyzed using the One-Way ANOVA test. P-value of <0.05 was considered statistically significant.

RESULTS

This study assessed the outcomes of pre-procedural antiplatelet regimens in CAS. Of 235 patients, 51.4% (n=121) received dual antiplatelet therapy (DAPT), 23.8% (n=56) received aspirin alone (SAPT-A), and 24.6% (n=58) received clopidogrel alone (SAPT-C). The mean age was 62.3±2.8 years for DAPT, 62.7±2.8 years for SAPT-A, and 63.2±3.2 years for SAPT-C (P=0.151). The average stenosis grade was 77.5±6.0% in DAPT, 74.0±7.2% in SAPT-A, and 75.2±7.1% in SAPT-C (P=0.069) (Table 1).

Primary Outcomes

At 30 days, stroke occurred in 0.8% of the DAPT group, significantly lower than 7.1% in SAPT-A and 6.9% in SAPT-C (P=0.047) (Table 2). TIA rates were also lower in DAPT (2.5%) compared to SAPT-A (12.5%) and SAPT-C (8.6%) (P=0.029). Myocardial infarction and 30-day mortality showed no significant group differences (P>0.05) (Fig. 1).

Secondary Outcomes

At six months, stent thrombosis rates were similar: 1.7% in DAPT, 1.8% in SAPT-A, and 1.7% in SAPT-C (P=0.998) (Table 3). Restenosis was seen in 4.1% of DAPT, 7.1% of SAPT-A, and 5.2% of SAPT-C patients (P=0.699). Stroke rates were 2.5% in DAPT, 8.9% in SAPT-A, and 8.6% in SAPT-C (P=0.108). Mortality rates did not differ significantly (P=0.446) (Fig. 2).

DISCUSSION

Atherosclerosis, characterized by arterial narrowing due to plaque buildup within vessel walls, is a major

Table 2. Month 1 results of patients according to antiplatelet use (Primary outcomes)

Variables		Antiplatelet usage			
		DAPT (n=121)	SAPT-A (n=56)	SAPT-C (n=58)	P value
Stroke 1st month	No	120	52	54	**0.047**†
	Yes	1	4	4	
TIA 1st month	No	118	49	53	**0.029**†
	Yes	3	7	5	
MI 1st month	No	120	55	56	0.446†
	Yes	1	1	2	
Bleeding	No	116	53	56	0.876†
	Yes	5	3	2	
Mortality 1st month	No	121	56	57	0.216†
	Yes	0	0	1	

DAPT=Dual Antiplatelet Therapy, SAPT-A=Single Antiplatelet Therapy-Aspirin, SAPT-C=Single Antiplatelet Therapy-Clopidogrel, TIA=Transient Ischemic Attack, MI=Myocardial Infarction

†Chi-Square Test

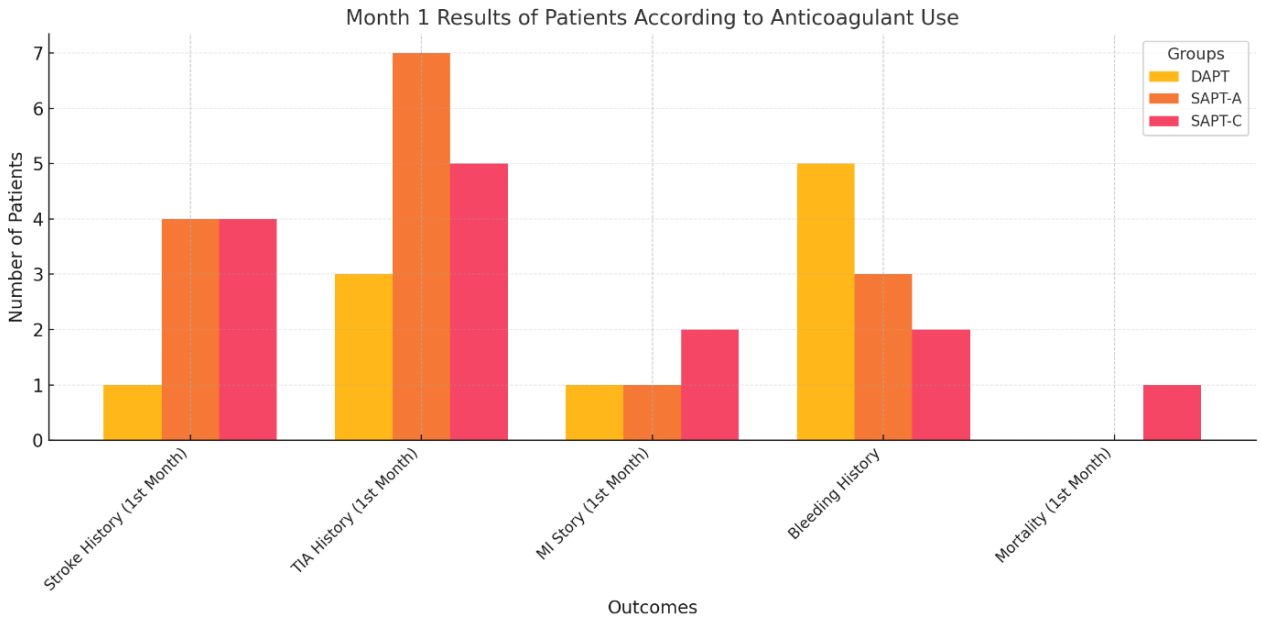

Fig. 1. Month 1 results of patients according to anticoagulant use.

contributor to cardiovascular disease [16], including carotid artery stenosis and its associated risks of ischemic events. Systemic atherosclerosis can lead to arterial occlusion, and advancements in treatment have shifted from surgical interventions to minimally invasive endovascular methods, which offer faster recovery and reduced complications [17, 18]. This study evaluated the effects of pre-procedural antiplatelet reg-

Table 3. Outcomes of patients at 6th month according to antiplatelet use (Secondary outcomes)

Variables		Antiplatelet usage			
		DAPT (n=121)	SAPT-A (n=56)	SAPT-C (n=58)	P value
Stent thrombosis	No	119	55	57	0.998†
	Yes	2	1	1	
Restenosis	No	116	52	55	0.699†
	Yes	5	4	3	
Stroke 6th month	No	118	51	53	0.108†
	Yes	3	5	5	
TIA 6th month	No	114	47	52	0.088†
	Yes	7	9	6	
MI 6th month	No	120	54	54	0.079†
	Yes	1	2	4	
Mortality 6th month	No	120	55	56	0.446†
	Yes	1	1	2	

DAPT=Dual Antiplatelet Therapy, SAPT-A=Single Antiplatelet Therapy-Aspirin, SAPT-C=Single Antiplatelet Therapy-Clopidogrel, TIA=Transient Ischemic Attack, MI=Myocardial Infarction

†Chi-Square Test

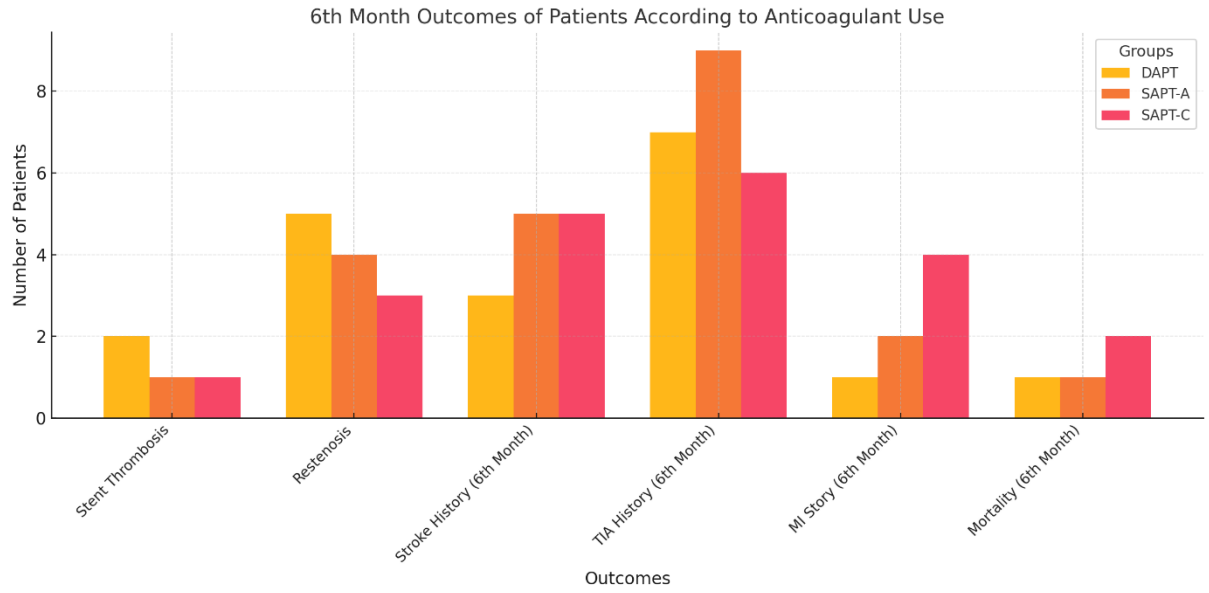

Fig. 2. 6th month outcomes of patients according to anticoagulant use.

imens on short- and long-term outcomes after CAS. The findings indicated that DAPT significantly reduced ischemic event risk while maintaining a favorable short-term safety profile. However, long-term outcomes did not differ between groups, likely due to the standard post-procedure DAPT regimen. Previous research supports the effectiveness of DAPT in preventing thrombotic events. The combination of aspirin and clopidogrel, in particular, has shown greater efficacy than single-agent therapies in reducing neurological complications [10, 11, 19]. The CARESS study demonstrated that dual antiplatelet therapy with clopidogrel and aspirin significantly lowered asymptomatic embolization rates, as detected by transcranial Doppler, in patients with recent symptomatic carotid stenosis. This finding highlights its superiority over aspirin monotherapy in high-risk patients [12]. Conversely, adding aspirin to clopidogrel in high-risk patients with ischemic events did not significantly improve vascular outcomes but notably increased the risk of major and life-threatening bleeding [20]. The MATCH study revealed that combining clopidogrel with aspirin provided no significant advantage over clopidogrel monotherapy in high-risk patients with recent ischemic events. However, the combination significantly elevated bleeding risk, limiting its use in this population [21]. Our study demonstrated that pre-procedural DAPT effectively reduced stroke and transient ischemic attack (TIA) rates in the short term. A significant reduction in these complications was observed in the DAPT group within the first month. No significant differences were observed among the groups regarding long-term outcomes. This homogeneity in long-term results may be attributed to the routine post-procedural administration of DAPT across all groups. On the other hand, differences in bleeding complications have been found depending on pre-procedural treatment, suggesting the need for individualization of the treatment regimen.

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) showed a two-year stroke incidence of 22% in patients with moderate carotid stenosis and 26% in those with severe stenosis [22].

The CREST study demonstrated that CEA and CAS had comparable clinical outcomes, with similar post-procedural complication rates (CAS: 7.6% vs. CEA: 6.4%, P=0.25) [23]. These findings confirm that CAS is a safe option for patients who are not suitable for surgery for anatomical or clinical reasons.

Our study aligns with these findings, highlighting the critical role of DAPT, particularly in preventing short-term ischemic events. In conclusion, this study underscores the need to optimize antiplatelet strategies for CAS. Dual antiplatelet therapy appears to be an effective approach for reducing short-term ischemic complications. However, larger prospective studies are necessary to refine individualized treatment regimens and assess their impact on long-term outcomes. These

results emphasize the importance of tailoring antiplatelet therapy to each patient and pave the way for developing new strategies to enhance the efficacy and safety of CAS.

Limitations

This study has several limitations. First, its retrospective design restricts the ability to establish causation, as data were collected from records, increasing the potential for missing or inaccurate information. Second, the study was conducted at a single center, limiting the findings' generalizability. Multi-center studies may yield results that are more representative of broader populations.

CONCLUSION

This study evaluated the impact of different antiplatelet regimens administered before CAS on short- and long-term clinical outcomes. The findings showed that DAPT significantly reduced short-term ischemic complications without compromising procedural safety. However, no notable differences were observed in long-term outcomes between the groups, likely due to the uniform post-procedural administration of DAPT.

These results underscore the importance of tailoring antiplatelet strategies for CAS. DAPT emerges as a beneficial approach for reducing short-term ischemic events in carefully selected patients. However, treatment plans should consider the potential risks, such as bleeding. Future research involving larger and more diverse populations with longer follow-up periods is necessary to further clarify the long-term effects of antiplatelet regimens. Such studies would strengthen the evidence base for optimizing the safety and efficacy of CAS.

Ethical Statement

This study was conducted in accordance with the ethical principles outlined in the 2008 Declaration of Helsinki. Ethical approval was obtained from the Zonguldak Bülent Ecevit University Clinical Research Ethics Committee (Approval No: 2024/22-1). All patient data were anonymized to ensure confidentiality and privacy.

Authors' Contribution

Study Conception: OA, MSG, EK; Study Design: OA, EK; Supervision: OA, EK; Funding: N/A; Materials: MSG, EK; Data Collection and/or Processing: OA, EK; Statistical Analysis and/or Data Interpretation: OA, EK; Literature Review: OA, MSG, EK; Manuscript Preparation: OA, MSG, EK and Critical Review: OA, MSG, EK.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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