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Research article

# One month follow-up of carotid endarterectomy with in-hospital preoperative aspirin monotherapy and postoperative dual antiplatelet therapy in asymptomatic and symptomatic patients: A multi-center study

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ABSTRACT

*Background:* There is currently no consensus regarding the optimal perioperative antiplatelet strategy for carotid artery surgery. This multicentre study aimed to analyse the association between preoperative aspirin monotherapy following postoperative dual antiplatelet therapy (DAPT) and the risk for stroke and death after carotid endarterectomy (CEA).

*Methods:* This cohort study included 821 patients with carotid artery stenosis who underwent CEA. Primary outcomes included any stroke or death up to the one-month postoperative follow-up. Multilevel multivariate regression analyses and descriptive statistics were performed.

*Results:* Patients were predominantly male (53 %), with a mean age of 66.2 years. The primary outcome occurred in 1.6 % of patients. Univariate and multivariate analyses revealed that patients with chronic obstructive pulmonary disease (COPD) exhibited a high risk for stroke or death ($P = 0.011$). The occurrence of any local complications in the neck was accompanied by an increase in diastolic blood pressure (DBP) ($P = 0.007$). Patients with a high systolic blood pressure (SBP) ($P = 0.002$) experienced a longer operative duration. The length of hospital stay was longer in the patients with COPD ($P = 0.020$), minor stroke ($P = 0.011$), and major stroke ($P = 0.001$). A positive linear correlation was found between SBP and operative duration in the overall population (β 0.4 [95 % confidence interval (CI) 0.1–0.7]; $P = 0.002$). The resultant curve for DBP and any local complications in the neck exhibited a two-stage change and one breakpoint in the entire population ($k = 68$ mmHg, <68; odds ratio [OR] 0.9 [95 % CI 0.7–1.1], $P = 0.461$; ≥68: OR 1.1 [95 % CI 1.0–1.1], $P = 0.003$).

*Conclusions:* Preoperative aspirin monotherapy and postoperative DAPT were safe and effective antiplatelet treatments for patients who underwent CEA.

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**Abbreviations**

| | |
|---|---|
| CEA | carotid Endarterectomy |
| CKD | chronic kidney disease |
| COPD | chronic obstructive pulmonary disease |
| DAPT | dual antiplatelet therapy |
| MI | myocardial infarction |
| mRS | modified Rankin scale |
| PSM | propensity score matching |
| SAPT | single antiplatelet therapy |
| TIA | transient ischemic attack |

## 1. Background

Carotid artery atherosclerosis contributes to approximately 18–25 % of ischemic strokes [1,2], while carotid artery stenosis has been implicated in an estimated 20 % of stroke and transient ischaemic attacks (TIA) [3]. Carotid endarterectomy (CEA) is an effective method of preventing ischaemic stroke caused by carotid stenosis [4]. The risk for periprocedural complications ranges from 3.6 % to 8.1 %, which include ischaemic stroke, death, or haemorrhage [4,5]. Evidence suggests that antiplatelet therapy can reduce the risk for stroke and TIA [6–8]. However, there is a risk for increased haemorrhagic complications, including hemorrhagic strokes, neck haematomas, and major bleeding, which must be considered [9,10].

Although medical management guidelines recommend dual antiplatelet therapy (DAPT) with aspirin and dipyridamole or clopidogrel for symptomatic patients and aspirin monotherapy for asymptomatic patients with atherosclerotic carotid artery disease [11,12]. There is currently no unanimous consensus regarding the optimal perioperative antiplatelet regimen for patients undergoing CEA [10,13,14]. The prescribing patterns for perioperative antiplatelet medications have been found to vary significantly among surgeons performing CEAs [15,16]. Despite the majority of surgeons not discontinuing aspirin before CEA, 43 % and 55 % would discontinue clopidogrel before CEA in both asymptomatic and symptomatic patients, respectively [16]. Special attention should be devoted to carotid stenosis subgroups (i.e., asymptomatic versus symptomatic). The second antiplatelet agent remains unclear whether it should be withheld preoperatively and resumed after surgery to reduce the risk for bleeding or continued throughout the perioperative period to decrease the risk for ischaemic complications. In our experience, preoperative aspirin monotherapy can reduce intraoperative bleeding, whereas postoperative DAPT can effectively prevent thrombosis and suppress intimal hyperplasia. As such, we performed a retrospective cohort study of perioperative and follow-up outcomes of CEA with regard to in-hospital preoperative aspirin monotherapy following postoperative DAPT. This study aimed to evaluate the current practice of antiplatelet therapy during CEA and risk for stroke or death.

## 2. Methods

### 2.1. Inclusion and exclusion criteria

This retrospective study aimed to evaluate the safety and efficacy of current antiplatelet therapies for management of CEA. Between January 2018 and December 2019, 945 patients underwent CEA in two high-level hospitals (Zhongshan Hospital affiliated with Fudan University and Changhai Hospital affiliated with PLA Naval Medical University, Shanghai, China). Patients who underwent elective surgery, defined as not emergent, such as crescendo TIA or stroke progression, were included in the study. Patients who underwent surgery for special conditions, such as carotid aneurysm, internal carotid artery (ICA) occlusion, and simultaneous cardiac or aortic surgery, those with allergy or intolerance to aspirin and/or clopidogrel, and individuals with incomplete documentation of clinical, demographic, and/or follow-up data were excluded. Patients included in the analysis were required to have started receiving aspirin monotherapy (100 mg/day) in the hospital before surgery and to be taking it up to the time of surgery. The perioperative period was defined as hospitalisation and/or hospitalisation within 14 days of the procedure. A flow diagram illustrating the inclusion and exclusion process is presented in Fig. 1. All included patients were treated with DAPT (aspirin [100 mg/day] + clopidogrel [75 mg/day]) postoperatively for one month and then treated with long-term aspirin monotherapy thereafter (100 mg/day).

### 2.2. Clinical and morphological variables

Data collected for the present study included the following: age; sex; neurological status on admission; type of index event (amaurosis fugax, TIA, minor or major stroke); ipsilateral and contralateral degrees of stenosis; preprocedural and postprocedural neurological assessment; surgical technique(s); shunt use; clamping time; and operative duration. Degree of carotid artery stenosis was quantified in accordance with the North American Symptomatic Carotid Endarterectomy Trial (i.e., "NASCET") method [17]. Symptomatic carotid stenosis was defined as the presence of neurological symptoms associated with ICA stenosis within the past 180 days. This classification was based on the most severe symptoms. Major stroke was defined as a score of 3–5 points on the modified Rankin Scale (mRS). Minor stroke was scored from 0 to 2 points on the mRS; other symptoms included anosmia, memory loss,

inarticulation, dizziness, and headache.

### 2.3. Outcome events

The primary outcomes were defined as any stroke or death following CEA during the follow-up period and subgroup analysis of symptomatic and asymptomatic patients. Secondary outcomes included any major stroke or death, TIA/stroke (mRS score 0–6), ipsilateral TIA/stroke, all-cause death, any local complications in the neck, cranial nerve palsy, residual stenosis, neck bleeding, nonoperative neck haematoma, and reoperation for bleeding. The diagnosis of neck haematoma was based on physical examination or ultrasonography. Local complications in the neck included cranial nerve palsy, residual stenosis, neck bleeding, and nonoperative neck haematoma. Other outcomes included operative duration, myocardial infarction (MI), and length of hospital stay.

### 2.4. Study collection

Due to the lack of a comparison group, a literature search for studies covering a span of nearly 10 years were included if they had a retrospective or prospective design that evaluated perioperative outcomes following CEA in patients undergoing single antiplatelet therapy (SAPT) and/or DAPT. Outcomes must have been reported as raw numbers and percentages. The perioperative period was defined as the same hospitalisation period or within 30 days of the procedure. The primary outcomes were stroke or death after CEA during the study period.

### 2.5. Analysis and statistics

No statistical method was used to estimate the sample size, and missing data were not analysed. Continuous variables are expressed as mean ± standard deviation (SD) and skewed variables are expressed as median and range, depending on distribution. Group comparisons were performed using the Student's *t*-test or Wilcoxon rank-sum test for numerical variables, and the chi-squared ($\chi^2$) or Fisher's exact test for categorical variables. Propensity score matching (PSM) was performed using an algorithm, with 1:2 matching based on age, sex, body mass index (BMI), and comorbid diseases to better account for the results and limit confounding from the measured covariates. To better explore the relationship between variables and operative duration/any local complications in the neck, smooth curve fitting and threshold effect analysis were performed. All analyses were performed using Empower (R) (www.empowerstats.com; X&Y Solutions, Inc., Boston, MA, USA) and R (http://www. R-project. org/). Differences with $P < 0.05$ were considered to be statistically significant, and factors with $P < 0.05$ in the univariate analysis were included in multivariate analysis.

## 3. Results

### 3.1. Patient characteristics

Between January 2018 and December 2019, 821 consecutive patients (435 male, 386 female; mean age, 66.2 years) were included in the analysis. A total of 653 (79.5 %) patients underwent surgery for symptomatic carotid stenosis and the remaining 168 (20.5 %) were treated for asymptomatic stenoses. Almost 86.0 % of patients exhibited severe (70%–99 %) carotid artery stenosis, and

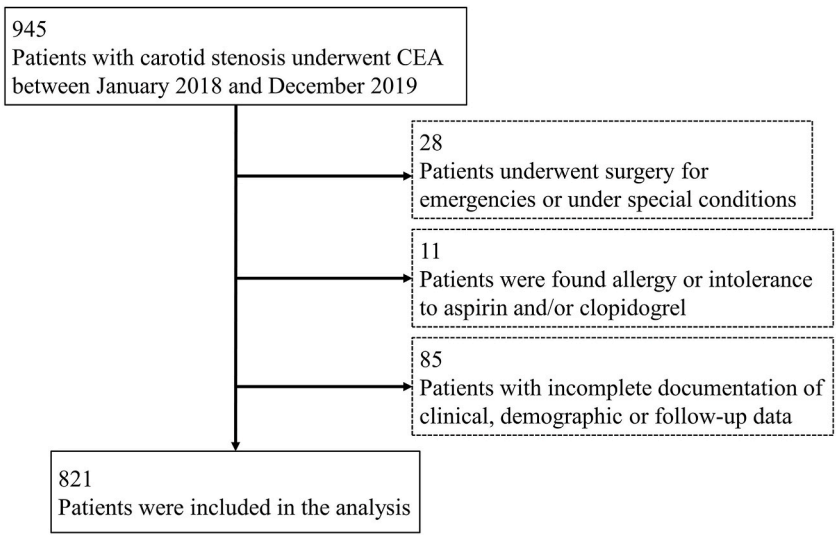


**Fig. 1.** Inclusion and exclusion criteria

**Table 1**
Demographic and clinical characteristics of study population.

| Patient demographics[a] | Entire Population | | | | Propensity Score Matched Population | | | |
|---|---|---|---|---|---|---|---|---|
| | Total (n = 821) | Symptomatic (n = 653) | ASymptomatic (n = 168) | *P*-value | Total (n = 411) | Symptomatic (n = 274) | ASymptomatic (n = 137) | *P*-value |
| Gender | | | | **< 0.001** | | | | **0.043** |
| Male | 435 (53.0 %) | 372 (57.0 %) | 63 (37.5 %) | | 206 (50.1 %) | 147 (53.6 %) | 59 (43.1 %) | |
| Female | 386 (47.0 %) | 281 (43.0 %) | 105 (62.5 %) | | 205 (49.9 %) | 127 (46.4 %) | 78 (56.9 %) | |
| Age,years | 66.2 ± 9.5 | 66.8 ± 8.9 | 64.0 ± 11.2 | **< 0.001** | 66.1 ± 9.0 | 66.1 ± 8.9 | 66.3 ± 9.2 | 0.834 |
| BMI,kg/m$^2$ | 25.1 ± 4.2 | 25.0 ± 4.1 | 25.5 ± 4.6 | 0.165 | 25.0 ± 4.4 | 24.9 ± 4.3 | 25.2 ± 4.6 | 0.621 |
| SBP,mmHg | 134.2 ± 15.6 | 134.1 ± 15.6 | 134.8 ± 15.6 | 0.580 | 134.7 ± 15.8 | 134.8 ± 15.6 | 134.4 ± 16.4 | 0.819 |
| DBP,mmHg | 78.1 ± 8.4 | 77.6 ± 8.3 | 79.9 ± 8.7 | **0.002** | 78.2 ± 8.8 | 77.9 ± 9.0 | 78.8 ± 8.4 | 0.301 |
| Ipsilateral degree of stenosis | | | | 0.894 | | | | 0.697 |
| Moderate (50%–69 %) | 115 (14.0 %) | 92 (14.1 %) | 23 (13.7 %) | | 62 (15.1 %) | 40 (14.6 %) | 22 (16.1 %) | |
| Severe (70%–99 %) | 706 (86.0 %) | 561 (85.9 %) | 145 (86.3 %) | | 349 (84.9 %) | 234 (85.4 %) | 115 (83.9 %) | |
| Contralateral degree of stenosis | | | | 0.716 | | | | 0.671 |
| Mild (<50 %) | 470 (57.2 %) | 376 (57.6 %) | 94 (56.0 %) | | 237 (57.7 %) | 159 (58.0 %) | 78 (56.9 %) | |
| Moderate (50%–69 %) | 303 (36.9 %) | 241 (36.9 %) | 62 (36.9 %) | | 150 (36.5 %) | 101 (36.9 %) | 49 (35.8 %) | |
| Severe (70%–99 %) | 48 (5.8 %) | 36 (5.5 %) | 12 (7.1 %) | | 24 (5.8 %) | 14 (5.1 %) | 10 (7.3 %) | |
| Hypertension | 571 (69.5 %) | 470 (72.0 %) | 101 (60.1 %) | **0.003** | 285 (69.3 %) | 186 (67.9 %) | 99 (72.3 %) | 0.364 |
| Hyperlipidemia | 51 (6.2 %) | 44 (6.7 %) | 7 (4.2 %) | 0.218 | 23 (5.6 %) | 16 (5.8 %) | 7 (5.1 %) | 0.762 |
| Diabetes | 223 (27.2 %) | 185 (28.3 %) | 38 (22.6 %) | 0.138 | 108 (26.3 %) | 72 (26.3 %) | 36 (26.3 %) | 1.000 |
| Coronary heart disease | 123 (15.0 %) | 95 (14.5 %) | 28 (16.7 %) | 0.493 | 62 (15.1 %) | 39 (14.2 %) | 23 (16.8 %) | 0.495 |
| Atrial fibrillation | 17 (2.1 %) | 14 (2.1 %) | 3 (1.8 %) | 0.771 | 10 (2.4 %) | 7 (2.6 %) | 3 (2.2 %) | 0.821 |
| COPD | 5 (0.6 %) | 4 (0.6 %) | 1 (0.6 %) | 0.979 | 3 (0.7 %) | 2 (0.7 %) | 1 (0.7 %) | 1.000 |
| CKD | 19 (2.3 %) | 14 (2.1 %) | 5 (3.0 %) | 0.522 | 8 (1.9 %) | 4 (1.5 %) | 4 (2.9 %) | 0.313 |
| Ipsilateral neuologic symptoms | 102 (12.4 %) | 100 (15.3 %) | 2 (1.2 %) | **< 0.001** | 17 (4.1 %) | 15 (5.5 %) | 2 (1.5 %) | 0.054 |
| History of neck radiation | 3 (0.4 %) | 3 (0.5 %) | 0 (0.0 %) | 0.379 | 3 (0.7 %) | 3 (1.1 %) | 0 (0.0 %) | 0.219 |
| MI history | 4 (0.5 %) | 3 (0.5 %) | 1 (0.6 %) | 0.822 | 3 (0.7 %) | 2 (0.7 %) | 1 (0.7 %) | 1.000 |
| Smoking | | | | 0.113 | | | | 0.577 |
| Never | 545 (66.4 %) | 423 (64.8 %) | 122 (72.6 %) | | 286 (69.6 %) | 187 (68.2 %) | 99 (72.3 %) | |
| Past | 104 (12.7 %) | 84 (12.9 %) | 20 (11.9 %) | | 57 (13.9 %) | 38 (13.9 %) | 19 (13.9 %) | |
| Current | 172 (21.0 %) | 146 (22.4 %) | 26 (15.5 %) | | 68 (16.5 %) | 49 (17.9 %) | 19 (13.9 %) | |
| Drinking | | | | **0.006** | | | | 0.833 |
| Never | 687 (83.7 %) | 532 (81.6 %) | 154 (91.7 %) | | 370 (90.0 %) | 245 (89.4 %) | 125 (91.2 %) | |
| Past | 22 (2.7 %) | 19 (2.9 %) | 3 (1.8 %) | | 11 (2.7 %) | 8 (2.9 %) | 3 (2.2 %) | |
| Current | 112 (13.6 %) | 101 (15.5 %) | 11 (6.5 %) | | 30 (7.3 %) | 21 (7.7 %) | 9 (6.6 %) | |
| Medication before admission | | | | | | | | |
| Stain | 440 (53.6 %) | 348 (53.3 %) | 92 (54.8 %) | 0.733 | 217 (52.8 %) | 147 (53.6 %) | 70 (51.1 %) | 0.625 |
| Antiplatelet | 552 (67.2 %) | 441 (67.5 %) | 111 (66.1 %) | 0.719 | 288 (70.1 %) | 196 (71.5 %) | 92 (67.2 %) | 0.361 |

(*continued on next page*)

**Table 1** (*continued*)

| Patient demographics[a] | Entire Population | | | | Propensity Score Matched Population | | | |
|---|---|---|---|---|---|---|---|---|
| | Total (n = 821) | Symptomatic (n = 653) | ASymptomatic (n = 168) | *P*-value | Total (n = 411) | Symptomatic (n = 274) | ASymptomatic (n = 137) | *P*-value |
| Anticoagulation | 172 (21.0 %) | 142 (21.7 %) | 30 (17.9 %) | 0.269 | 82 (20.0 %) | 218 (79.6 %) | 111 (81.0 %) | 0.727 |
| β-blockers | 100 (12.2 %) | 76 (11.6 %) | 24 (14.3 %) | 0.349 | 46 (11.2 %) | 28 (10.2 %) | 18 (13.1 %) | 0.376 |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; MI, myocardial infarction.

[a] Categorical data are shown as number (%) and continuous data as mean ± standard deviation.

approximately 5.8 % of all patients exhibited severe contralateral stenosis. PSM was performed to evaluate the primary outcomes and minimise the effect of measured confounders on patient demographics and comorbidities. Population data obtained from these analyses are summarised in Table 1.

### 3.2. Perioperative and intraoperative management

The most common surgical technique used was conventional carotid endarterectomy (69.3 %), followed by eversion (30.7 %). Routine or selective shunting was performed in 1.2 % of patients. The mean clamping time was 17.8 min and the mean operative duration was 145.1 min. More details regarding surgical management and PSM results are summarised in Table 2.

### 3.3. Perioperative and one-month follow-up outcomes

Primary outcomes included stroke or in-hospital death in 13 (1.6 %) patients. With antiplatelet therapy, the risk for stroke or death was 1.7 % in symptomatic and 1.2 % in asymptomatic patients. Major stroke or death was recorded in 0.9 % of all patients, and 0.9 % and 0.6 % of symptomatic and asymptomatic patients, respectively. Outcomes were distributed as follows: any TIA/stroke (mRS score 0–6), 1.9 %; ipsilateral TIA/stroke, 1.7 %; death, 0.2 %; any local complications in the neck, 3.8 %; cranial nerve palsy, 2.2 %; residual stenosis, 0.4 %; neck bleeding, 0.9 %; nonoperative neck haematoma, 0.7 %; and reoperation for bleeding in 0.4 %. More details and PSM results are summarised in Table 3.

### 3.4. High risk factors for outcomes

Univariate regression analysis revealed a significant association with a higher risk for any stroke or death in COPD (odds ratio [OR] 16.7 [95 % confidence interval (CI) 1.7–161.2]; P = 0.015). The incidence of any local complications in the neck increased with age (β

**Table 2**
Perioperative and intraoperative management.

| Entire Population | | | | |
|---|---|---|---|---|
| Management[a] | Total (n = 821) | Symptomatic (n = 653) | ASymptomatic (n = 168) | *P*-value |
| Operation technique | | | | < **0.001** |
| Conventional | 569 (69.3 %) | 432 (66.2 %) | 137 (81.5 %) | |
| Eversion | 252 (30.7 %) | 221 (33.8 %) | 31 (18.5 %) | |
| Shunt use | 10 (1.2 %) | 4 (0.6 %) | 6 (3.6 %) | **0.002** |
| Intraoperative bleeding volume/ml | 62.8 ± 66.1 | 63.1 ± 68.1 | 61.5 ± 58.2 | 0.785 |
| Clamping time, min | 17.8 ± 7.8 | 17.6 ± 7.8 | 18.8 ± 7.7 | 0.079 |
| Duration of operation, min | 145.1 ± 53.1 | 145.2 ± 53.9 | 144.7 ± 50.0 | 0.922 |
| Postoperative drainage volume/ml | 23.5 ± 23.3 | 22.9 ± 20.7 | 25.7 ± 31.6 | 0.160 |
| Length of stay,day | 9.8 ± 7.0 | 10.1 ± 7.6 | 8.5 ± 3.3 | 0.074 |
| Propensity Score Matched Population | | | | |
| Management[a] | Total (n = 411) | Symptomatic (n = 274) | ASymptomatic (n = 137) | *P*-value |
| Operation technique | | | | **0.002** |
| Conventional | 289 (70.3 %) | 179 (65.3 %) | 110 (80.3 %) | |
| Eversion | 122 (29.7 %) | 95 (34.7 %) | 27 (19.7 %) | |
| Shunt use | 8 (1.9 %) | 2 (0.7 %) | 6 (4.4 %) | **0.012** |
| Intraoperative bleeding volume/ml | 60.1 ± 60.6 | 58.7 ± 60.0 | 62.7 ± 61.7 | 0.533 |
| Clamping time, min | 18.2 ± 7.6 | 17.9 ± 7.6 | 19.0 ± 7.7 | 0.155 |
| Duration of operation, min | 146.4 ± 53.6 | 148.2 ± 55.2 | 142.7 ± 50.3 | 0.326 |
| Postoperative drainage volume/ml | 23.9 ± 28.6 | 22.7 ± 25.0 | 26.5 ± 34.7 | 0.200 |
| Length of stay,day | 9.5 ± 4.5 | 9.9 ± 4.8 | 8.8 ± 3.5 | **0.012** |

[a] Categorical data are shown as number (%) and continuous data as mean ± standard deviation.

1.0 [95 % CI 0.9–1.0]; P = 0.029), diastolic blood pressure (DBP) (β 1.1 [95 % CI 1.0–1.1]; P = 0.008) and minor stroke (OR 2.3 [95 % CI 1.1–4.6; P = 0.027). Patients with COPD experienced a higher intraoperative bleeding volume (β 63.6 [95 % CI 5.6–121.6]; P = 0.032) and longer length of hospital stay (β 7.4 [95 % CI 1.3–13.6]; P = 0.018). Operative duration was significantly increased among patients with high systolic blood pressure (SBP) (β 0.4 [95 % CI 0.2–0.7]; P < 0.001). Patients with symptomatic carotid stenosis (β 1.6 [95 % CI 0.4–2.8]; P = 0.008), minor stroke (β 1.6 [95 % CI 0.6–2.7; P = 0.002), or major stroke (β 5.1 [95 % CI 1.8–8.5]; P = 0.003) also had a longer length of hospital stay. More details and PSM results are summarised in Table 4.

Further multivariate analyses were performed to identify important independent factors, and were adjusted for in the model, including: age; BMI; sex; SBP; DBP; hypertension; hyperlipidaemia; diabetes; coronary artery disease; atrial fibrillation; COPD; chronic kidney disease; history of neck radiation; history of MI; smoking; alcohol consumption; stain; antiplatelet; anticoagulation; β-blockers; indication; minor stroke (mRS score 0–2); and major stroke (mRS score 3–5). Patients with COPD (OR 36.7 [95 % CI 2.3–593.4]; P = 0.011) still exhibited an obvious high risk for any stroke or death. The occurrence of any local complications in the neck was accompanied by an increase in DBP (OR 1.1 [95 % CI 1.0–1.1]; P = 0.007), other than age or minor stroke. Intraoperative bleeding volume increased in patients with COPD (β 63.3 [95 % CI 3.8–122.8]; P = 0.037), and the opposite was true for patients with minor stroke (β −13.9 [95 % CI -24.5 to −3.2]; P = 0.011). However, in these PSM evaluations, no interaction was observed between intraoperative bleeding volume and COPD or minor stroke. Patients with a high SBP (β 0.4 [95 % CI 0.1–0.7]; P = 0.002) had a longer operative duration. Moreover, the length of hospital stay was longer in patients with COPD (β 7.4 [95 % CI 1.2–13.7]; P = 0.020), minor stroke (β 1.5 [95 % CI 0.3–2.6]; P = 0.011) and major stroke (β 5.6 [95 % CI 2.2–9.0]; P = 0.001). More details and PSM results are presented in Table 5.

After adjusting for possible confounding factors, smooth curve fitting and threshold effect analyses were performed to explore these relationships. A positive linear correlation was found between SBP and operative duration whether in the overall (β 0.4 [95 % CI 0.1–0.7]; P = 0.002) or PSM (β 0.5 [95 % CI 0.2–0.9]; P = 0.004) populations. The resultant curve for DBP and any local complications in the neck exhibited a two-stage change and one breakpoint in the overall population (k = 68 mmHg, <68: OR 0.9 [95 % CI 0.7–1.1], P = 0.461; ≥68, OR 1.1 [95 % CI 1.0–1.1]; P = 0.003). An increasing trend was also observed in the PSM population, although there were large differences among the individuals (Fig. 2).

### 3.5. Comparison of results with international studies

Seven studies from the literature were included for comparison. Preoperative aspirin and postoperative DAPT were empirical anticoagulation strategies used at the authors' institution, which differed from other studies. Therefore, complications in symptomatic and asymptomatic patients were compared. In addition to stroke or death, neck haematoma, a common complication described in these studies, is shown in Table 6. Compared with previous studies, this study demonstrated that preoperative aspirin and

**Table 3**
Postoperative neurologic or local complications until one month follow-up.

| Entire Population | | | | |
|---|---|---|---|---|
| Outcomes[a] | Total (n = 821) | Symptomatic (n = 435) | Asymptomatic (n = 386) | *P*-value |
| Any stroke or death | 13 (1.6 %) | 11 (1.7 %) | 2 (1.2 %) | 0.647 |
| Any major stroke or death | 7 (0.9 %) | 6 (0.9 %) | 1 (0.6 %) | 0.684 |
| Any TIA/Stroke (mRS, 0–6) | 16 (1.9 %) | 13 (2.0 %) | 3 (1.8 %) | 0.864 |
| Ipsilateral TIA/Stroke | 14 (1.7 %) | 11 (1.7 %) | 3 (1.8 %) | 0.928 |
| Death | 1 (0.2 %) | 1 (0.2 %) | 0 (0.0 %) | 0.544 |
| Any local complications on the neck | 31 (3.8 %) | 28 (4.3 %) | 3 (1.8 %) | 0.129 |
| Cranial nerve palsy | 18 (2.2 %) | 17 (2.6 %) | 1 (0.6 %) | 0.113 |
| Residual-stenosis | 3 (0.4 %) | 2 (0.3 %) | 1 (0.6 %) | 0.580 |
| Neck bleeding | 7 (0.9 %) | 7 (1.1 %) | 0 (0.0 %) | 0.178 |
| Non-operative neck haematoma | 6 (0.7 %) | 5 (0.8 %) | 1 (0.6 %) | 0.817 |
| Reoperation for bleeding | 3 (0.4 %) | 3 (0.5 %) | 0 (0.0 %) | 0.379 |
| Propensity Score Matched Population | | | | |
| Outcomes[a] | Total (n = 411) | Symptomatic (n = 274) | ASymptomatic (n = 137) | *P*-value |
| Any stroke or death | 6 (1.5 %) | 5 (1.8 %) | 1 (0.7 %) | 0.383 |
| Any major stroke or death | 3 (0.7 %) | 2 (0.7 %) | 1 (0.7 %) | 1.000 |
| Any TIA/Stroke (mRS, 0–6) | 7 (1.7 %) | 5 (1.8 %) | 2 (1.5 %) | 0.787 |
| Ipsilateral TIA/Stroke | 7 (1.7 %) | 5 (1.8 %) | 2 (1.5 %) | 0.787 |
| Death | 0 | 0 | 0 | N/A |
| Any local complications on the neck | 18 (4.4 %) | 16 (5.8 %) | 2 (1.5 %) | **0.041** |
| Cranial nerve palsy | 11 (2.7 %) | 10 (3.6 %) | 1 (0.7 %) | 0.084 |
| Residual-stenosis | 1 (0.2 %) | 1 (0.4 %) | 0 | 0.479 |
| Neck bleeding | 2 (0.5 %) | 2 (0.7 %) | 0 | 0.316 |
| Non-operative neck haematoma | 4 (1.0 %) | 3 (1.1 %) | 1 (0.7 %) | 0.722 |
| Reoperation for bleeding | 0 | 0 | 0 | N/A |

TIA, transient ischemic attack; mRS, modified Rankin scale.
[a] Categorical data are shown as number (%).

**Table 4**
Univariate regression analysis for postoperative complications (Non-adjusted).

| Entire Population | | | | | |
|---|---|---|---|---|---|
| Variable | Any stroke or death[b] | Any local complications[b] | Intraoperative bleeding volume[a] | Duration of operation[a] | Length of stay[a] |
| Age | 1.0 (0.9, 1.0) 0.286 | **1.0 (0.9, 1.0) 0.029** | 0.3 (−0.2, 0.8) 0.235 | −0.2 (−0.6, 0.2) 0.282 | 0.0 (0.0, 0.1) 0.651 |
| SBP | 1.0 (1.0, 1.0) 0.674 | 1.0 (1.0, 1.0) 0.826 | 0.1 (−0.2, 0.4) 0.499 | **0.4 (0.2, 0.7) < 0.001** | 0.0 (−0.0, 0.0) 0.947 |
| DBP | 1.0 (1.0, 1.1) 0.464 | **1.1 (1.0, 1.1) 0.008** | −0.1 (−0.6, 0.4) 0.721 | 0.4 (−0.0, 0.8) 0.073 | 0.0 (−0.0, 0.1) 0.213 |
| COPD | **16.7 (1.7, 161.2) 0.015** | N/A | **63.6 (5.6, 121.6) 0.032** | 6.0 (−40.7, 52.7) 0.802 | **7.4 (1.3, 13.6) 0.018** |
| Symptomatic | 1.4 (0.3, 6.5) 0.649 | 2.5 (0.7, 8.2) 0.142 | 1.6 (−9.7, 12.8) 0.785 | 0.5 (−8.6, 9.5) 0.922 | **1.6 (0.4, 2.8) 0.008** |
| Minor stroke (mRS, 0–2) | 2.4 (0.8, 7.3) 0.116 | **2.3 (1.1, 4.6) 0.027** | −9.4 (−19.0, 0.2) 0.055 | 6.8 (−0.9, 14.5) 0.083 | **1.6 (0.6, 2.7) 0.002** |
| Major stroke (mRS, 3–5) | 4.1 (0.5, 33.7) 0.186 | 3.6 (0.8, 16.3) 0.102 | −4.7 (−36.4, 27.1) 0.774 | 2.8 (−22.7, 28.3) 0.829 | **5.1 (1.8, 8.5) 0.003** |
| Propensity Score Matched Population | | | | | |
| Variable | Any stroke or death[b] | Any local complications[b] | Intraoperative bleeding volume[a] | Duration of operation[a] | Length of stay[a] |
| Age | 0.9 (0.9, 1.0) 0.102 | **1.0 (0.9, 1.0) 0.046** | 0.2 (−0.4, 0.9) 0.486 | 0.1 (−0.5, 0.7) 0.707 | −0.0 (−0.1, 0.0) 0.653 |
| SBP | 1.0 (0.9, 1.0) 0.893 | 1.0 (1.0, 1.0) 0.251 | 0.2 (−0.2, 0.5) 0.390 | **0.6 (0.3, 0.9) < 0.001** | 0.0 (−0.0, 0.0) 0.816 |
| DBP | 1.0 (0.9, 1.1) 0.785 | **1.1 (1.0, 1.1) 0.016** | −0.3 (−1.0, 0.4) 0.410 | 0.6 (−0.0, 1.1) 0.066 | **0.1 (0.0, 0.1) 0.013** |
| COPD | **40.3 (3.1, 520.0) 0.005** | N/A | 3.3 (−65.6, 72.2) 0.925 | −17.5 (−78.4, 43.4) 0.573 | **14.2 (9.3, 19.1) < 0.001** |
| Symptomatic | 2.5 (0.3, 21.8) 0.399 | 4.2 (0.9, 18.5) 0.059 | −4.0 (−16.4, 8.5) 0.533 | 5.5 (−5.5, 16.5) 0.326 | **1.2 (0.3, 2.1) 0.012** |
| Minor stroke (mRS, 0–2) | 2.8 (0.6, 14.0) 0.214 | 1.8 (0.7, 4.7) 0.241 | −4.6 (−17.8, 8.6) 0.495 | 10.9 (−0.8, 22.6) 0.068 | **2.5 (1.5, 3.4) < 0.001** |
| Major stroke (mRS, 3–5) | **16.0 (1.6, 163.0) 0.019** | 4.6 (0.5, 41.3) 0.176 | −22.0 (−70.9, 26.8) 0.377 | −12.1 (−55.3, 31.2) 0.585 | 3.2 (−0.4, 6.8) 0.085 |

SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; OR, odds ratio.
[a] *β (95%CI) Pvalue.*
[b] *OR (95%CI) Pvalue.*

postoperative DAPT were safe and effective antiplatelet treatments for CEA.

## 4. Discussion

CEA is commonly performed in patients undergoing SAPT or DAPT to decrease the risk for stroke related to carotid stenosis [15,16]. The surgeon must decide whether to continue or discontinue antiplatelet agents before CEA to balance the haemorrhagic and ischaemic risks associated with the procedure. However, there is no uniform strategy for perioperative antiplatelet therapy across different departments of vascular surgery, and the optimal antiplatelet strategy remains unclear. This multicentre study was designed to evaluate the safety and effectiveness of preoperative aspirin monotherapy following DAPT and the risk for stroke and death after CEA compared with the current antiplatelet strategies in other studies.

At our institution, patient preoperative hospital length of stay is usually 3–5 days. Temporary SAPT can effectively prevent recurrent cerebral ischaemic events and does not increase intraoperative bleeding. Although CEA removes plaques and vascular intima, it remains a traumatic procedure, and local inflammatory reactions can promote the formation of mural thrombi. However, SAPT monotherapy is insufficient; therefore, postoperative DAPT was implemented. DAPT effectively prevents thrombosis and inhibits carotid restenosis caused by short-term intimal hyperplasia. To prevent other possible future bleeding events, patients are asked to switch to SAPT. A recent study reported a significantly increased risk for neck bleeding in patients who underwent CEA and undergoing DAPT, but no difference in TIA, stroke, or death rates compared with SAPT [14]. This finding demonstrates that SAPT is sufficient for preventing perioperative stroke. Based on our experience, preoperative aspirin monotherapy is used for acute stroke prevention and decreased perioperative bleeding compared with DAPT, while postoperative DAPT is used to prevent carotid thrombosis and remote stroke. The perioperative and follow-up results revealed that the risk for stroke or death was lower in our patients (1.6 %) than in those without perioperative antiplatelet therapy (2.0 %) in a recent study [14]. Moreover, consistent with several previous studies, DAPT after surgery was associated with a low risk for postoperative death [10,24]. One patient, 65 years of age, with severe COPD and a history of major stroke died of pulmonary infectious complications that were not associated with the study treatment. This suggests that the use of preoperative aspirin monotherapy and postoperative DAPT is an effective preventive strategy for serious adverse events, including stroke or death, after CEA.

**Table 5**
Multivariate regression analysis for postoperative complications.

| Entire Population | | | | | |
|---|---|---|---|---|---|
| Variable | Any stroke or death[b] | Any local complications[b] | Intraoperative bleeding volume[a] | Duration of operation[a] | Length of stay[a] |
| Age | 1.0 (0.9, 1.0) 0.388 | 1.0 (0.9, 1.0) 0.112 | 0.2 (−0.4, 0.7) 0.542 | −0.3 (−0.7, 0.1) 0.157 | 0.0 (−0.0, 0.1) 0.648 |
| SBP | 1.0 (1.0, 1.0) 0.992 | 1.0 (1.0, 1.0) 0.494 | 0.1 (−0.2, 0.4) 0.443 | **0.4 (0.1, 0.7) 0.002** | −0.0 (−0.0, 0.0) 0.560 |
| DBP | 1.0 (0.9, 1.0) 0.645 | **1.1 (1.0, 1.1) 0.007** | −0.1 (−0.6, 0.5) 0.829 | 0.1 (−0.4, 0.5) 0.824 | 0.0 (−0.0, 0.1) 0.147 |
| COPD | **36.7 (2.3, 593.4) 0.011** | N/A | **63.3 (3.8, 122.8) 0.037** | 7.1 (−40.6, 54.8) 0.770 | **7.4 (1.2, 13.7) 0.020** |
| Symptomatic | 1.1 (0.2, 8.1) 0.899 | 2.5 (0.6, 10.7) 0.214 | 9.3 (−3.1, 21.8) 0.141 | 1.7 (−8.2, 11.7) 0.731 | 0.8 (−0.5, 2.1) 0.230 |
| Minor stroke (mRS, 0–2) | 2.4 (0.6, 10.3) 0.239 | 1.8 (0.8, 4.3) 0.175 | **−13.9 (-24.5, -3.2) 0.011** | 6.9 (−1.7, 15.4) 0.116 | **1.5 (0.3, 2.6) 0.011** |
| Major stroke (mRS, 3–5) | 6.5 (0.5, 80.6) 0.145 | 2.8 (0.5, 17.5) 0.264 | −10.7 (−43.1, 21.8) 0.519 | 8.1 (−17.9, 34.1) 0.542 | **5.6 (2.2, 9.0) 0.001** |
| Propensity Score Matched Population | | | | | |
| Variable | Any stroke or death[b] | Any local complications[b] | Intraoperative bleeding volume[a] | Duration of operation[a] | Length of stay[a] |
| Age | 0.9 (0.7, 1.0) 0.042 | 1.0 (0.9, 1.0) 0.091 | −0.2 (−0.9, 0.5) 0.586 | −0.2 (−0.8, 0.5) 0.606 | 0.0 (−0.0, 0.0) 0.971 |
| SBP | 1.0 (0.9, 1.0) 0.356 | 1.0 (0.9, 1.0) 0.165 | 0.2 (−0.2, 0.6) 0.384 | **0.5 (0.2, 0.9) 0.003** | −0.0 (−0.0, 0.0) 0.467 |
| DBP | 1.0 (0.9, 1.1) 0.840 | **1.1 (1.0, 1.2) 0.005** | −0.3 (−1.0, 0.4) 0.411 | 0.3 (−0.3, 1.0) 0.300 | **0.1 (0.0, 0.1) 0.023** |
| COPD | **232.8 (2.8, 19642.5) 0.016** | N/A | 8.3 (−61.6, 78.2) 0.816 | −19.7 (−80.0, 40.5) 0.521 | **13.5 (8.7, 18.2) < 0.001** |
| Symptomatic | 1.1 (0.0, 26.9) 0.948 | 6.1 (1.0, 37.9) 0.052 | 0.1 (−14.0, 14.2) 0.988 | 5.3 (−6.9, 17.4) 0.397 | 0.1 (−0.8, 1.1) 0.787 |
| Minor stroke (mRS, 0–2) | 4.2 (0.2, 73.9) 0.331 | 1.4 (0.4, 5.1) 0.567 | −1.7 (−17.2, 13.7) 0.825 | 7.0 (−6.4, 20.4) 0.305 | **2.2 (1.1, 3.3) < 0.001** |
| Major stroke (mRS, 3–5) | **276.6 (3.2, 23944.6) 0.013** | 2.0 (0.2, 25.2) 0.604 | −15.0 (−65.5, 35.5) 0.561 | −4.5 (−48.0, 39.0) 0.840 | 3.1 (−0.4, 6.5) 0.080 |

SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; OR, odds ratio.
Adjust for: Age; BMI; Gender; SBP; DBP; Hypertension; Hyperlipidemia; Diabetes; Coronary artery disease; Atrial fibrillation; COPD; CKD; History of neck radiation; MI history; Smoking; Drink; Stain use; Antiplatelet; Anticoagulation; β-blockers; Indication; Minor stroke (mRS, 0–2); Major stroke (mRS, 3–5).
[a] *β (95%CI) Pvalue.*
[b] *OR (95%CI) Pvalue.*

Previous studies from China have revealed that males account for a higher proportion of patients with atherosclerotic carotid stenosis in the country [25,26]. Our findings were in accordance with these results in that males predominated among the enrolled patients (53.0 %) and were more likely to be symptomatic (57 %), with a similar trend observed in the PSM population. There was no direct explanation as to why symptomatic patients were mostly male. We speculate that this may be related to smoking, drinking, or poor dietary habits. Conventional CEA remains the primary surgical modality at our centre, and a shunt was only used in several patients with severe stenosis. Symptomatic patients experienced a prolonged length of hospital stay compared with asymptomatic patients in the PSM population, although no significant difference was found in the overall sample. This indicates that patients with symptomatic carotid stenosis may be at a relatively high risk for postoperative complications.

Several studies have recommended DAPT and SAPT for asymptomatic stenosis [11,12]. In our study, preoperative aspirin monotherapy and postoperative DAPT were administered to all patients, without distinguishing between those who were symptomatic and asymptomatic. The present study focused only on the outcomes of different antiplatelet strategies but neglected the difference between symptomatic and asymptomatic patients. Therefore, a subgroup analysis of symptomatic versus asymptomatic carotid stenosis was performed. However, the postoperative and follow-up results did not reveal obvious differences, except for any local complications in the neck in the PSM population. Symptomatic patients exhibited a high risk for local complications in the neck, possibly due to more severe carotid stenosis, which may increase the technical difficulty of the surgery.

Univariate and multivariate regression analyses revealed several important independent factors associated with postoperative complications. COPD has been confirmed to be associated with an increased risk for mortality in many diseases, such as carotid stenosis [10][1] and hemorrhagic stroke [27] among others. In our study, patients with COPD or major stroke with perceived poor physical health may have resulted in an increased risk for postoperative stroke. Interestingly, high DBP, especially >68 mmHg, was associated with an increased odds of local complications in the neck, which could also result in prolonged hospitalisation. Otherwise, elevated SBP was associated with a longer operative duration. Therefore, we recommend maintaining a relatively low perioperative blood pressure in patients who undergo CEA, which would help improve prognosis. In contrast to the results for the overall population, the effect of COPD and minor stroke on intraoperative bleeding volume was not significant in the PSM group. However, larger prospective clinical studies aimed at confirming our findings are warranted.

Results regarding bleeding complications after carotid surgery using SAPT and DAPT are controversial. Whereas one study demonstrated that patients underwent carotid surgery with DAPT exhibited a 5-fold increase in bleeding risk, another retrospective

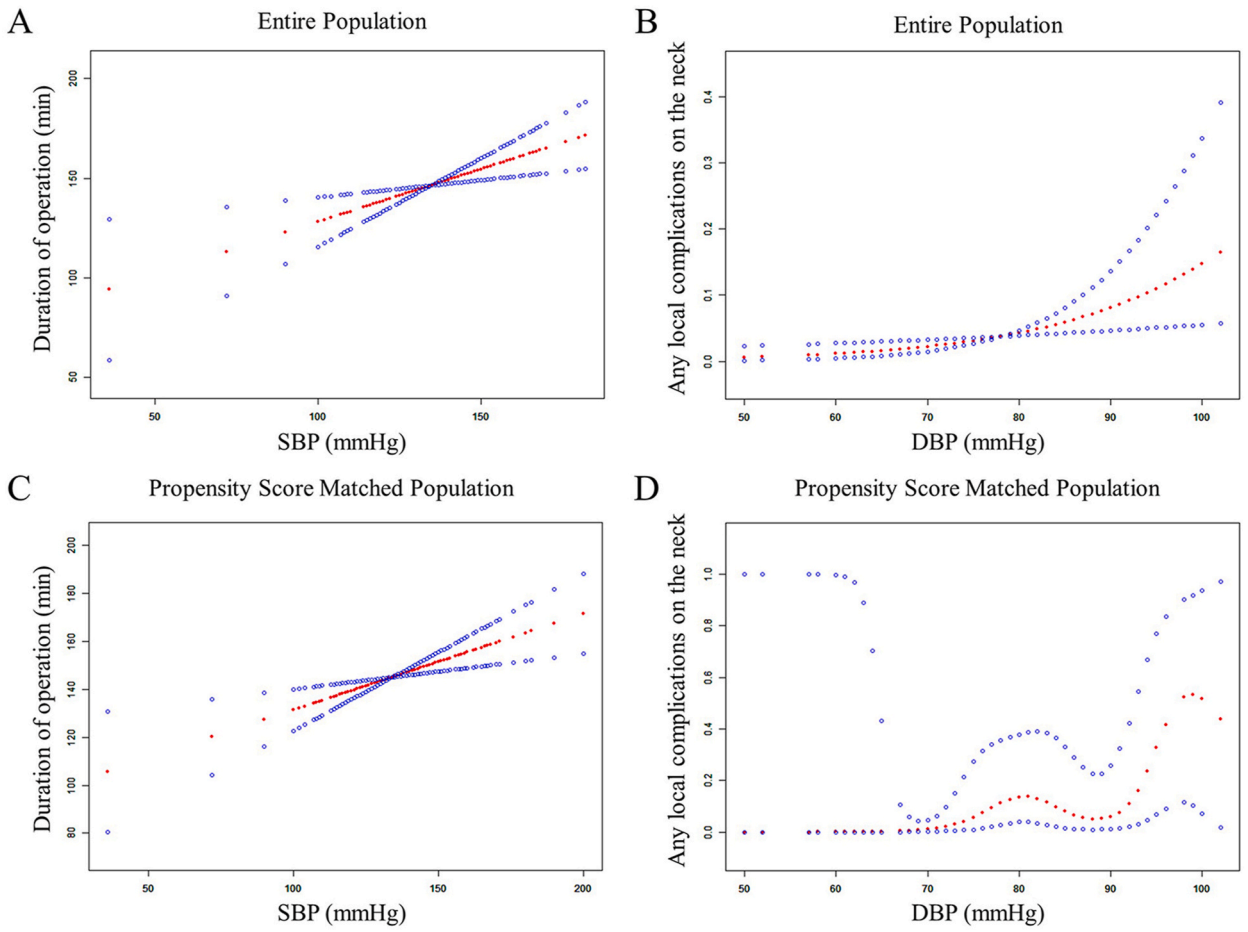


**Fig. 2.** The smooth curve fitting results.A. The graph displays the adjusted association between baseline SBP and duration of operation in entire population. B. The graph displays the adjusted association between baseline DBP and any local complication on the neck in entire population. C. The graph displays the adjusted association between baseline SBP and duration of operation in PSM population. D. The graph displays the adjusted association between baseline DBP and any local complication on the neck in PSM population. The model adjusted for Age, BMI, Gender, SBP, DBP, Hypertension, Hyperlipidemia, Diabetes, Coronary artery disease, Atrial fibrillation, COPD, CKD, History of neck radiation, MI history, Smoking, Drink, Stain use, Antiplatelet, Anticoagulation, β-blockers, Indication, Minor stroke (mRS, 0-2), Major stroke (mRS, 3-5).

**Table 6**
Comparison of our own results with the international studies.

| Studies | Antiplatelet regimen | Any stroke or death (%) | Neck haematoma (%) |
|---|---|---|---|
| Payne et al. (2004) [18] | Pre-op Clopidogrel + Aspirin/Placebo + Aspirin | 1 (2.2 %)/1 (1.9 %) | 6 (13.0 %)/3 (5.6 %) |
| Sharpe et al. (2010) [19] | Aspirin/Clopidogrel + Aspirin | 27 (3.3 %)/10 (3.7 %) | N/A |
| Chechik et al. (2012) [20] | NO/Clopidogrel/Clopidogrel + Aspirin | 3 (3.7 %)/0/2 (12.5 %) | 4 (4.9 %)/0/1 (6.3 %) |
| Oldag et al. (2012) [21] | Aspirin/Clopidogrel/Clopidogrel + Aspirin | N/A | 48 (11.7 %)/33 (20.4 %)/27 (24.1 %) |
| Hale et al. (2013) [22] | NO/Aspirin/Clopidogrel + Aspirin | N/A | 6 (1.2 %)/4 (0.9 %)/14 (4.4 %) |
| Chisci et al. (2016) [23] | SAPT/DAPT | 8 (0.8 %)/3 (1.4 %) | 18 (2.0 %)/3 (3.8 %) |
| Jones et al. (2016) [10] | Aspirin/Clopidogrel + Aspirin | 206 (1.0 %)/57 (0.8 %) | N/A |
| Zimmerman et al. (2018) [14] | NO/Aspirin/SAPT, others/DAPT | 227 (2.0 %)/1722 (1.8 %)/50 (1.5 %)/111 (1.9 %) | 340 (3.0 %)/2098 (2.1 %)/127 (3.9 %)/252 (4.4 %) |
| Glotzer et al. (2021) [24] | SAPT/DAPT | 4 (1.6 %)/16 (1.3 %) | 7 (2.9 %)/29 (2.4 %) |
| Current research | Pre-op Aspirin and Post-op DAPT | Sym 11 (1.7 %)/Asym 2 (1.2 %) | Sym 5 (0.8 %)/Asym 1 (0.6 %) |

study reported no significant difference between SAPT and DAPT [22,28]. Two previous meta-analyses revealed that DAPT did not decrease the occurrence of stroke or death in major CEA outcomes but increased the risk for bleeding [29,30]. Evidence suggests that postoperative neck haematoma is associated with adverse cardiac events, neurological complications, increased operative mortality,

and cranial nerve injuries [31]. Hence, efforts to reduce the risk for neck haematomas are warranted. Our results demonstrated that this antiplatelet strategy significantly decreased the rate of postoperative neck haematomas, and the risk for stroke or death remained at an acceptably low level compared with several previous studies. The results also indicated the importance of antiplatelet therapy in the perioperative setting despite the lack of dose-response curves.

## 5. Limitations

This is a limited experience on the application of "an empirical anticoagulation strategy" applied in two referral Chinese hospital, which can however be useful as a proposal for further research.

## 6. Conclusions

Compared with previous studies, preoperative aspirin monotherapy and postoperative DAPT were associated with a relatively low risk for perioperative stroke and death during the one-month follow-up, even in patients with symptomatic carotid stenosis. This antiplatelet therapeutic strategy was safe and effective in those undergoing CEA.

## Ethics approval and consent to participate

Ethical approval to report this study was obtained from the ethical committee of Zhongshan Hospital and Changhai Hospital. All methods were carried out in accordance with relevant guidelines and regulations.

## Consent for publication

All named authors have agreed to the publication of the work.

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## Data availability statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

## CRediT authorship contribution statement

**Tonglei Han:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Hanfei Tang:** Writing – review & editing, Writing – original draft, Validation, Project administration, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Changpo Lin:** Writing – review & editing, Writing – original draft, Validation, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Jiaqi Zhu:** Validation, Investigation, Data curation. **Yang Shen:** Validation, Investigation, Data curation. **Dong Yan:** Validation, Investigation, Data curation. **Zhiqing Zhao:** Validation, Project administration, Formal analysis, Data curation, Conceptualization. **Jiang Lin:** Validation, Formal analysis. **Bin Gao:** Validation, Investigation, Data curation. **Yi Si:** Validation, Investigation, Data curation. **Xiaolong Wei:** Validation, Investigation, Data curation. **Xiao Tang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Daqiao Guo:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Weiguo Fu:** Validation, Investigation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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