Stroke

CLINICAL AND POPULATION SCIENCES

Determinants and Temporal Trends of Dual Antiplatelet Therapy After Mild Noncardioembolic Stroke

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BACKGROUND: Short-term dual antiplatelet therapy (DAPT) reduces early stroke recurrence after mild noncardioembolic ischemic stroke (NCIS). We aim to evaluate temporal trends and determinants of DAPT prescription after mild NCIS in the Florida Stroke Registry, a statewide registry across Get With The Guidelines-Stroke participating hospitals.

METHODS: In this cross-sectional analysis of a cohort study, we included patients with mild NCIS (National Institutes of Health Stroke Scale score ≤3) who were potentially eligible for DAPT across 168 Florida Stroke Registry participating hospitals between January 2010 and September 2022. Using antiplatelet prescription as the dependent variable (DAPT versus single antiplatelet therapy), we fit logistic regression models adjusted for patient-related factors, hospital-related factors, clinical presentation, vascular risk factors, and ischemic stroke subtype, to obtain adjusted odds ratios (aORs) with 95% CIs.

RESULTS: From 283 264 Florida Stroke Registry ischemic stroke patients during the study period, 109 655 NCIS were considered eligible. Among these, 37 058 patients with National Institutes of Health Stroke Scale score >3 were excluded, resulting in a sample of 72 597 mild NCIS (mean age 68±14 years; female 47.3%). Overall, 24 693 (34.0%) patients with mild NCIS were discharged on DAPT and 47 904 (66.0%) on single antiplatelet therapy. DAPT prescription increased from 25.7% in 2010 to 52.8% in 2022 (β/year 2.5% [95% CI, 1.5%–3.4%]). Factors associated with DAPT prescription were premorbid antiplatelet therapy (aOR, 4.66 [95% CI, 2.20–9.88]), large-artery atherosclerosis (aOR, 1.68 [95% CI, 1.43–1.97]), diabetes (aOR, 1.29 [95% CI, 1.13–1.47]), and hyperlipidemia (aOR, 1.24 [95% CI, 1.10–1.39]), whereas female sex (aOR, 0.83 [95% CI, 0.75–0.93]), being non-Hispanic Black patients (compared with non-Hispanic White patients; aOR, 0.78 [95% CI, 0.68–0.90]), admission to a Thrombectomy-capable Stroke Center (compared with Comprehensive Stroke Center; aOR, 0.78 [95% CI, 0.66–0.92]), time-to-presentation 1 to 7 days from last seen well (compared with <24 h; aOR, 0.86 [95% CI, 0.76–0.96]), and small-vessel disease stroke (aOR, 0.81 [95% CI, 0.72–0.94]) were associated with not receiving DAPT at discharge.

CONCLUSIONS: Despite a temporal trend increase in DAPT prescription after mild NCIS, we found substantial underutilization of evidence-based DAPT associated with significant disparities in stroke care.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: aspirin ■ atherosclerosis ■ clopidogrel ■ hyperlipidemia ■ ischemic stroke

The early phase after an ischemic stroke has the highest risk of recurrence and is a critical period to institute effective antithrombotic therapy.[1] For patients with noncardioembolic ischemic stroke (NCIS) presenting with mild neurological deficits (National Institutes of Health Stroke Scale [NIHSS] score ≤3), 2 independent

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Nonstandard Abbreviations and Acronyms

aOR	adjusted odds ratio
CHANCE	Clopidogrel in High-Risk Patients With Acute Nondisabling Cerebrovascular Events
CLAIR	Clopidogrel Plus Aspirin Versus Aspirin Alone for Reducing Embolization in Patients With Acute Symptomatic Cerebral or Carotid Artery Stenosis
DAPT	dual antiplatelet therapy
FSR	Florida Stroke Registry
GWTG-S	Get With The Guidelines-Stroke
NCIS	noncardioembolic ischemic stroke
NIHSS	National Institutes of Health Stroke Scale
POINT	Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke
SAMMPRIS	Stenting Versus Aggressive Medical Therapy for Intracranial Arterial Stenosis
SAPT	single antiplatelet therapy
SPS3	Secondary Prevention of Small Subcortical Strokes

randomized clinical trials (CHANCE [Clopidogrel in High-Risk Patients With Acute Nondisabling Cerebrovascular Events] and POINT [Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke])[2,3] established the superiority of short-term dual antiplatelet therapy (DAPT) with aspirin plus clopidogrel compared with single antiplatelet therapy (SAPT) with aspirin. Pooled analyses of these trials estimated that DAPT initiated within 24 hours of symptoms onset resulted in ≈30% decreased 90-day risk of ischemic stroke recurrence, mainly in the first 21 days.[4,5] Published in 2019, the American Heart Association/American Stroke Association (AHA/ASA) guidelines incorporated a class 1 (level of evidence A) recommendation for short-term DAPT with aspirin and clopidogrel to reduce the 90-day risk of stroke in this population.[6] Several international medical societies have mirrored this evidence-based recommendation.[7–9]

Although high-quality evidence has emerged and influenced treatment guidelines, recent studies indicate incomplete DAPT implementation after mild NCIS.[10,11] It is fundamental to understand the factors that determine antiplatelet therapy selection to develop strategies to expand the uptake of guidelines recommendations. In the Florida Stroke Registry (FSR), we sought to evaluate the temporal trends of DAPT utilization after mild NCIS, independent of the time-to-presentation. Additionally, we aimed to examine the impact of CHANCE, POINT, and the updated AHA/ASA guidelines on DAPT usage, and identify factors contributing to DAPT prescription disparities.

METHODS

As FSR uses data from AHA/ASA Get With The Guidelines-Stroke (GWTG-S), and data-sharing agreements require an application process at www.heart.org/qualityresearch to be considered by the AHA publication committee. Investigators followed the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) reporting guidelines.[12]

Study Population

FSR is a statewide registry including GWTG-S participating hospitals. The overall aim of the registry is to identify stroke care disparities and develop programs to improve stroke care quality in Florida.[13,14] From 2010 to 2017, the registry comprised GWTG-S participating hospitals from Florida and Puerto Rico, was known as the Florida–Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD), and was funded by the National Institute of Neurological Disorders.[13,14] Since 2017, the registry continues as the FSR with funding support from the state of Florida (COHAN-R3).

In this cross-sectional analysis of a cohort study, we analyzed data from January 2010 to September 2022 across 168 FSR participating hospitals. By September 2022, the 168 FSR participating hospitals represented >95% of total stroke centers in the state. Briefly, deidentified information for patients with the primary diagnosis of stroke was collected by trained personnel using standard GWTG-S questionnaires, and additional FSR-specific inquires on patient's demographics, clinical presentation, and hospital characteristics. This study was approved by the University of Miami institutional review board. Each participating hospital received institutional ethics approval to enroll patients in the registry without requiring individuals' consent under the common rule or a waiver of authorization and exemption from subsequent review by the institutional review board.

The current analysis was restricted to patients with final diagnosis of acute ischemic stroke with mild deficits at presentation as defined by initial NIHSS score 0 to 3, independent of the time-to-presentation. Figure 1 details the study inclusion and exclusion criteria. The main outcome was DAPT prescription with aspirin and clopidogrel at discharge, while the comparison group were those discharged on SAPT with either aspirin or clopidogrel alone. Therefore, we excluded those who were discharged on systemic anticoagulation, antiplatelet combinations other than the aforementioned, or were not prescribed any antiplatelet therapy at discharge. The latter group was excluded due to the likelihood that antiplatelet therapy was not prescribed due to contraindications related to active bleeding, infarct hemorrhagic transformation, or considered high bleeding risk.

Variables of Interest

Admission date was recorded to analyze DAPT prescription temporal trends. Additionally, variables of interest were identified using data collected on an interactive internet-based patient management tool. Patient-related factors included age at presentation, sex, race/ethnicity by self-identification, and

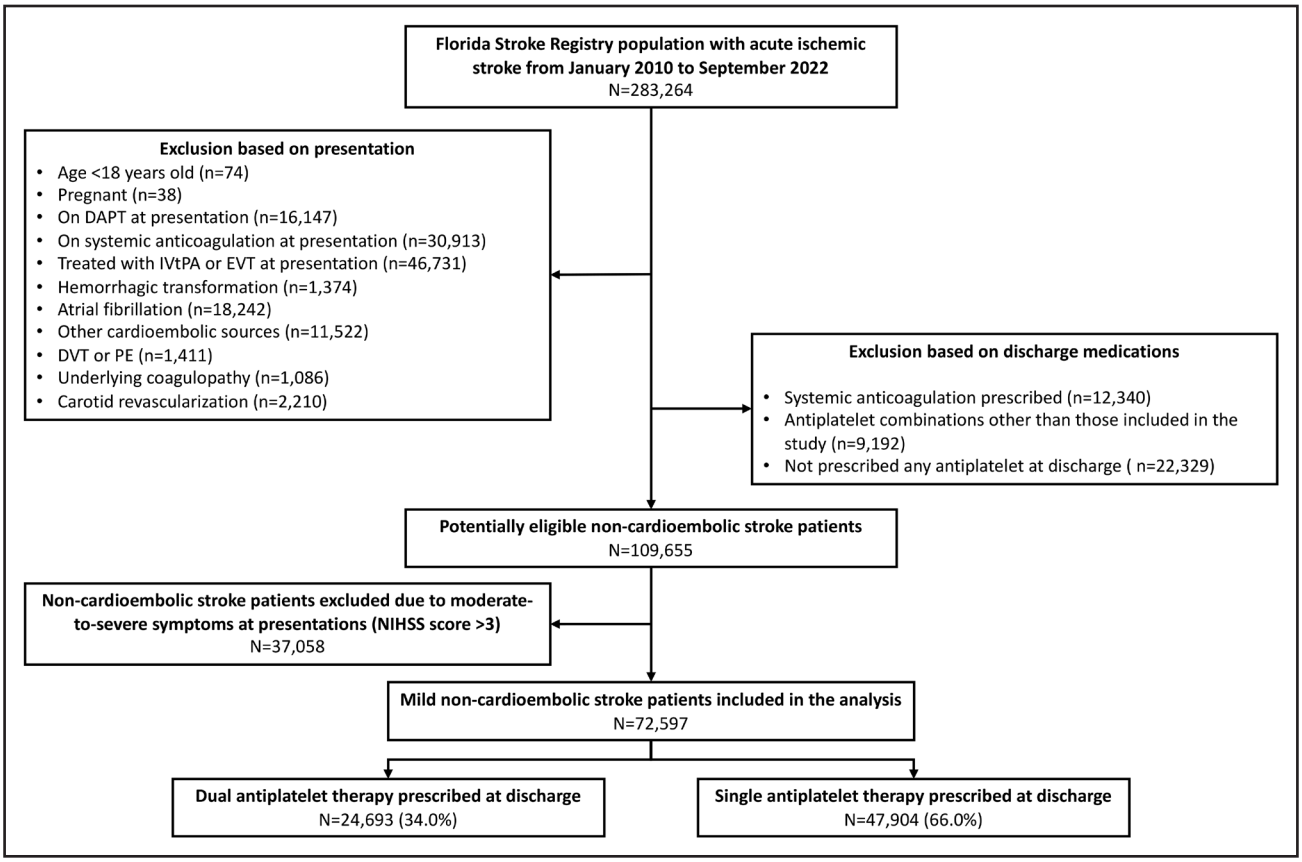

Figure 1. Flowchart of the study population.
DAPT indicates dual antiplatelet therapy; DVT, deep venous thrombosis; EVT, endovascular therapy; IVtPA, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; and PE, pulmonary embolism.

insurance status. Hospital-related factors included academic affiliation, stroke center certification, and rural versus urban location. Clinical presentation factors included time to-presentation calculated by subtracting the time of arrival minus the time of last known well, and categorized as <24 hours, 1 to 7 days and >7 days, antiplatelet therapy at the time of the index event, and initial NIHSS score. Vascular risk factors included history of hypertension, diabetes, hyperlipidemia, and current smoking status. Stroke subtype was categorized based on the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification.[15]

Statistical Analysis

Linear regression analysis using DAPT prescription percentage as the dependent variable and the year of presentation as the independent variable were used to estimate temporal trends. Additionally, we used 1-sided 2-sample *Z* test for equality of proportions comparing all-cases before and after the publication of CHANCE (July 2013),[2] POINT (July 2018),[3] and the AHA/ASA guidelines (October 2019)[6] to determine the difference in the proportion of DAPT prescription. To investigate whether variables of interest correlated with DAPT prescription, we fit serial logistic regression models to obtain adjusted odds ratios (aORs) with 95% CIs. The first model (model 1) was adjusted for patient- and hospital-related factors based on our hypothesis that odds of receiving DAPT prescription would differ based on the social determinants of health and result in healthcare disparities. The subsequent model (model 2) incorporated clinical presentation and vascular risk factors to account for their potential impact on physicians' antiplatelet therapy selection. Most variables had <5% missing values, except for time-to-presentation (18.9%). Only patients with nonmissingness for these variables were included in the aforementioned models. In model 3, stroke subtype was included as a potential factor determining antiplatelet therapy choice. Due to the significant missingness for stroke subtype variable (53.4%), we present results using 2 different approaches: the complete case approach (model 3a) and the missing indicator approach (model 3b). Additionally, we performed sensitivity analyses in the subgroup of patients who presented <24 hours of last seen well, and those admitted after AHA/ASA guidelines publication to test whether study variables associated with DAPT prescription remained unchanged. Data management and analysis were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Out of 283 264 FSR ischemic stroke patients enrolled during the study period, 109 655 NCIS were considered eligible. Among these, 37 058 nonmild NCIS (NIHSS score >3) were excluded, resulting in a final sample of 72 597 mild NCIS patients discharged on either DAPT or SAPT (Figure 1). Excluded antiplatelet combinations are summarized in Table S1. The study population mean

age was 68±14 years and 47.3% were women. Overall, 24 693 (34.0%) patients were discharged on DAPT with aspirin and clopidogrel, and 47 904 (66.0%) on SAPT (aspirin 39 075 [53.8%] and clopidogrel 8829 [12.2%]). Study population baseline characteristics stratified by antiplatelet therapy are summarized in Table 1. Time-to-presentation was available in 60 631 patients, from which 40 424 (66.7%) presented <24 hours of last seen well. Within this group, 13 946 (34.5%) patients were discharged on DAPT and 26 478 (65.5%) on SAPT (aspirin 21 467 [81.1%] and clopidogrel 5011 [18.9%]).

During the initial study period (2010–2012), there were no major variations in DAPT prescription. From 2013 (year of CHANCE publication), there was a progressive surge in DAPT prescription (β/year 2.5% [95% CI, 1.5%–3.4%]), increasing from 18.3% in 2013 to 52.8% in 2022 (Figure 2A). The difference in proportions from before-and-after CHANCE, POINT, and the 2019 AHA/ASA guidelines increased by 13.9%, 18.3%, and 19.6%, respectively (P<0.01 for all calculations). Similarly, temporal trends revealed progressive DAPT prescription increase in the subgroup of patients presenting <24 hours of last seen well (Figure 2B).

In multivariate analysis adjusted for patient- and hospital-related factors (model 1), DAPT prescription compared with SAPT was associated with older age and admission to academic hospitals, while not being prescribed DAPT was associated with female sex, non-Hispanic Black and Hispanic race-ethnicity (compared with non-Hispanic White patients), and Thrombectomy-Capable Stroke Center certification (compared with Comprehensive Stroke Center). After further adjusting for clinical presentation, vascular risk factors and stroke subtype (model 3a), female sex (aOR, 0.83 [95% CI, 0.75–0.93]), non-Hispanic Black patients (compared with non-Hispanic White patients; aOR, 0.78 [95% CI, 0.68–0.90]), and Thrombectomy-Capable Stroke Center certification (compared with Comprehensive Stroke Center; aOR, 0.78 [95% CI, 0.66–0.92]) remained associated with not being prescribed DAPT. Additionally, DAPT prescription was more frequent among those with large-artery atherosclerosis stroke (aOR, 1.68 [95% CI, 1.43–1.97]), premorbid antiplatelet therapy (aOR, 4.66 [95% CI, 2.20–9.88]), diabetes (aOR, 1.29 [95% CI, 1.13–1.47]) and hyperlipidemia (aOR, 1.24 [95% CI, 1.10–1.39]), and less frequent in those presenting 1 to 7 days from last seen well (compared with <24 hours; aOR, 0.86 [95% CI, 0.76–0.96]), and small-vessel disease stroke (aOR, 0.81 [95% CI, 0.72–0.94]; Table 2). Study results remained similar after using the missing indicator approach for stroke subtype variable (Model 3b; Table S2). Sensitivity analyses in those who presented <24 hours of last seen well and those enrolled after AHA/ASA 2019 guidelines publication did not alter study results significantly (Tables S3 and S4).

Table 1. Baseline Study Population Characteristics Stratified by Whether Dual Antiplatelet Therapy or Single Antiplatelet Therapy Were Prescribed at Discharge

	Total (n=72 597)	SAPT (n=47 904)	DAPT (n=24 693)
Patient-related factors			
Age, y; mean (SD)	68 (14)	68 (14)	69 (13)
Female sex, %	47.3	48.6	44.5
Race/ethnicity, %			
Non-Hispanic White	71.9	69.4	75.5
Non-Hispanic Black	20.7	21.7	18.6
Hispanic	6	7.5	4.5
Asian	1.2	1.2	1.2
Other	0.1	0.1	0.2
Health insurance, %			
Private	34.4	34.4	35.1
Medicare	44.3	43.4	45.2
Medicaid	4.9	4.9	4.7
Self/none	16.5	17.4	15
Hospital-related factors			
Academic affiliation, %	25.3	24.2	25.9
Stroke center certification, %			
Comprehensive stroke center	46.5	46.6	45.6
Thrombectomy stroke capable	13.3	13.7	12.6
Primary stroke center	38.7	37.7	40.9
Acute stroke ready hospital	0.3	0.3	0.4
None	1.1	1.7	0.5
Rural location, %	0.5	0.5	0.4
Clinical presentation factors			
Time to presentation			
<24 h	66.7	66.6	66.8
1–7 d	30.4	30.6	30.0
>7 d	2.9	2.8	3.2
Antiplatelet use before presentation, %	4.7	4.3	5.7
Initial NIHSS score, median (IQR)	1 (2)	1 (2)	1 (2)
Stroke subtype, %			
Large-artery atherosclerosis	17.4	14.6	21.1
Small vessel disease	39.9	42.6	36.8
Other determined cause	3.7	3.9	3.2
Cryptogenic	39	38.9	39
Vascular risk factors			
Hypertension, %	75.9	72.9	81.5
Diabetes, %	36.2	33.4	40.6
Hyperlipidemia, %	58.1	54.3	65.3
Current smoker, %	19.2	19.5	18.8

DAPT indicates dual antiplatelet therapy; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; and SAPT, single antiplatelet therapy.

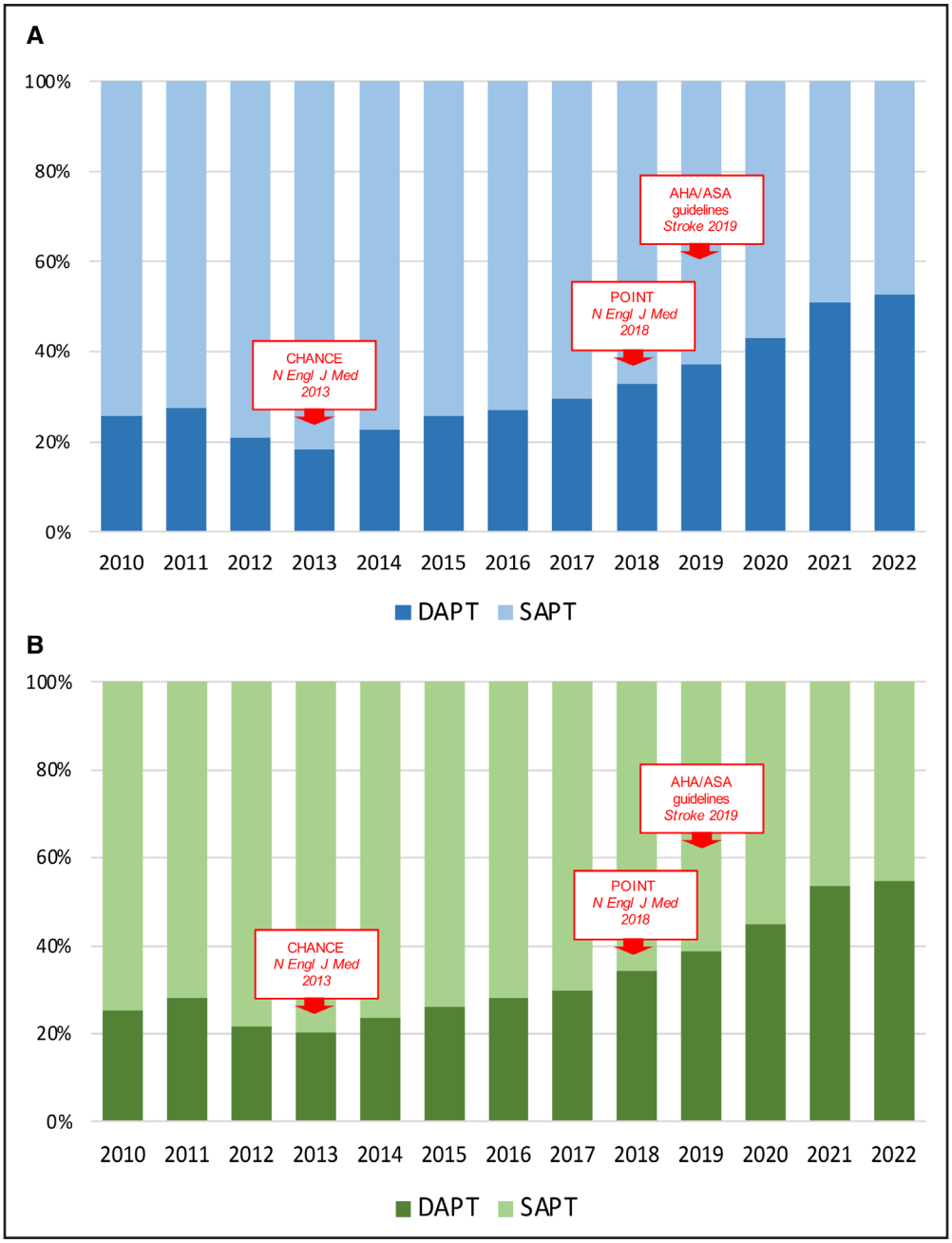

Figure 2. Time trends of the use of dual antiplatelet therapy after mild noncardioembolic stroke in the Florida Stroke Registry population from January 2010 to September 2022.
A, All-inclusive analysis; (**B**) subgroup of patients who presented <24 h of last seen well. DAPT indicates dual antiplatelet therapy; and SAPT, single antiplatelet therapy.

DISCUSSION

In a large sample of mild NCIS patients enrolled in a statewide stroke registry over more than a decade, we found that DAPT prescription compared with SAPT increased over time in relation to the publication of pivotal clinical trials and the updated AHA/ASA guidelines. However, over half of the study patients were not discharged on evidence-based DAPT, even after the AHA/ASA guidelines publication. Our study highlights significant stroke care disparities demonstrating that women and non-Hispanic Black patients, and those admitted to a Thrombectomy-Capable Stroke Center, were less likely to receive recommended DAPT. Additionally, DAPT prescription was influenced by clinical characteristics including stroke subtype, higher vascular risk profile, and having a stroke while on antiplatelet therapy.

FSR findings align with US national data across GTWG-S participating hospitals that showed significant underutilization of DAPT after mild NCIS.[10,16] DAPT was

Table 2. Multivariable Analyses on the Factors Associated With Dual Antiplatelet Prescription at Discharge in Patients With Acute Mild Noncardioembolic Ischemic Stroke

	Unadjusted analysis		Model 1		Model 2		Model 3a	
	OR (95% CI)		aOR (95% CI)		aOR (95% CI)		aOR (95% CI)	
Patient-related factors								
Age (per 10 y)	1.01	(1.01–1.01)*	1.01	(1.00–1.02)	1.00	(0.99–1.01)	1.00	(0.99–1.01)
Female sex	0.85	(0.83–0.89)*	0.82	(0.78–0.86)*	0.83	(0.75–0.92)*	0.83	(0.75–0.93)*
Race/ethnicity								
Non-Hispanic White (reference)	…	…	…	…	…	…	…	…
Non-Hispanic Black	0.78	(0.75–0.81)*	0.82	(0.78–0.87)*	0.77	(0.67–0.88)*	0.78	(0.68–0.90)*
Hispanic	0.38	(0.33–0.44)*	0.82	(0.68–0.98)*	0.85	(0.59–1.23)	0.85	(0.59–1.24)
Asian	0.91	(0.78–1.07)	0.96	(0.79–1.17)	0.74	(0.50–1.11)	0.76	(0.51–1.14)
Other	1.21	(0.80–1.83)	1.61	(0.94–2.74)	0.88	(0.26–3.02)	0.92	(0.27–3.17)
Health insurance								
Private (reference)	…	…	…	…	…	…	…	…
Medicare	1.04	(1.00–1.08)	1.03	(0.98–1.09)	1.11	(0.96–1.27)	1.08	(0.94–1.24)
Medicaid	0.94	(0.86–1.03)	0.98	(0.88–1.10)	0.87	(0.69–1.11)	0.86	(0.68–1.09)
Self/none	0.85	(0.81–0.90) *	0.99	(0.92–1.06)	0.99	(0.85–1.15)	0.99	(0.85–1.15)
Hospital-related factors								
Academic affiliation	1.11	(1.06–1.15)*	1.15	(1.08–1.22)*	1.07	(0.95–1.21)	1.10	(0.97–1.24)
Stroke center certification								
Comprehensive stroke center (reference)	…	…	…	…	…	…	…	…
Thrombectomy stroke capable	0.94	(0.89–0.99)*	0.69	(0.64–0.75)*	0.80	(0.68–0.95)*	0.78	(0.66–0.92)*
Primary stroke center	1.18	(1.13–1.22)*	0.94	(0.87–1.01)	1.04	(0.92–1.18)	1.05	(0.93–1.19)
Acute stroke ready hospital	1.36	(1.03–1.80)*	0.81	(0.60–1.08)	0.81	(0.38–1.73)	0.82	(0.38–1.76)
None	0.97	(0.52–1.78)	0.99	(0.38–2.57)	0.99	(0.07–2.56)	0.77	(0.31–1.87)
Rural location	1.68	(1.08–2.62)*	1.30	(0.59–2.88)	1.82	(0.40–8.17)	1.45	(0.32–6.58)
Clinical presentation factors								
Time to presentation								
<24 h (reference)	…	…			…	…	…	…
1–7 d	0.98	(0.94–1.02)			0.85	(0.76–0.96)*	0.86	(0.76–0.96)*
>7 d	1.12	(1.00–1.25)			1.04	(0.79–1.36)	1.01	(0.77–1.32)
Premorbid antiplatelet therapy	1.64	(1.51–1.79)*			4.73	(2.24–9.98)*	4.66	(2.20–9.88)*
Initial NIHSS	0.99	(0.98–1.01)			0.98	(0.93–1.03)	0.98	(0.93–1.03)
Vascular risk factors								
Hypertension	1.60	(1.53–1.67)*			1.06	(0.95–1.20)	1.08	(0.96–1.22)
Diabetes	1.34	(1.29–1.38)*			1.29	(1.13–1.47)*	1.29	(1.13–1.47)*
Hyperlipidemia	1.58	(1.53–1.64)*			1.24	(1.11–1.40)*	1.24	(1.10–1.39)*
Current smoker	1.03	(0.99–1.08)			1.05	(0.93–1.20)	1.06	(0.93–1.21)
Stroke subtype								
Cryptogenic (reference)	…	…					…	…
Large-artery atherosclerosis	1.53	(1.42–1.64)*					1.68	(1.43–1.97)*
Small vessel disease	0.86	(0.82–0.91)*					0.81	(0.72–0.92)*
Other determined cause	0.81	(0.71–0.91)*					1.06	(0.83–1.36)

Model 1: adjusted for age at presentation, sex, race/ethnicity, health insurance, academic affiliation, stroke center certification, and rural vs urban location. Model 2: adjusted for age at presentation, sex, race/ethnicity, health insurance, academic affiliation, stroke center certification, rural vs urban location, time-to-presentation, premorbid antiplatelet therapy, initial NIHSS, hypertension, diabetes, hyperlipidemia, and smoking status. Model 3a: adjusted for covariates in model 2 plus stroke subtype using the complete case approach. aOR indicates adjusted odds ratio; and NIHSS, National Institutes of Health Stroke Scale.

*P value <0.05.

also reported in advanced stroke centers in China, where only one-third of mild NCIS received evidence-based DAPT.[17] However, determinants of DAPT prescription were not fully addressed in the aforementioned studies. Our study provides novel insights in the factors associated with antiplatelet therapy selection after mild NCIS. We found notable disparities based on sex and race-ethnicity, and these disparities persisted after accounting for clinical presentation and vascular risk factors. Moreover, the sensitivity analysis conducted on individuals who presented <24 hours from last seen well and those enrolled after AHA/ASA guidelines publication yielded similar results. This suggests that the observed disparities remained unchanged among patients who fell within level 1A guideline recommendations. The US national data among GWTG-S hospitals from 2003 to 2008 have identified that women and non-Hispanic Black patients are less likely to receive stroke care key performance measures including intravenous thrombolysis, antithrombotic therapy within 48 hours, deep venous thrombosis prophylaxis within 48 hours, antithrombotic therapy at discharge, statin therapy at discharge, anticoagulation for atrial fibrillation, and smoking cessation counseling.[18,19] More recent data from the FSR (2010–2014) concur with US national data in that women are less likely to receive stroke defect-free care,[14] while non-Hispanic Black paitents only differed by less smoking cessation counseling.[13] Furthermore, the FSR identified that women and non-Hispanic Black individuals were more likely to receive delayed acute stroke care including longer door-to-needle and door-to-CT times.[20,21] Our findings add to the aforementioned data showing that women and minority groups tend to receive suboptimal stroke care, and suggest that antiplatelet therapy selection in the acute phase may contribute further to the higher readmission and mortality rates reported in these populations.[22,23] Quality improvement interventions have shown to be effective improving adherence to stroke care performance metrics and to reduce disparities.[24,25] Therefore, integrating evidence-based DAPT prescription as a stroke care metric along with quality improvement interventions such as GWTG-Stroke represent a promising opportunity to mitigate or minimize disparities in stroke care delivery.

In our study, Thrombectomy-Capable Stroke Center compared with Comprehensive Stroke Center certification was associated with lower likelihood of DAPT prescription, while academic hospitals showed a trend toward higher DAPT prescription. These hospital-related differences were more evident after AHA/ASA guidelines publication. It is well-documented that higher levels of certification associate with greater stroke care quality and improved outcomes.[26,27] Our results support that hospitals with better established stroke care systems are more likely to treat mild NCIS in accordance to evidence-based recommendations. In addition, specialist consultation access may be particularly important, as demonstrated by a survey across emergency medicine physicians that showed that only 6% of practitioners would start DAPT early after a mild NCIS.[11] Similar to disparities related to sex and race-ethnicity, implementing hospital-level quality improvement interventions on evidence-based DAPT prescription has the potential to be a meaningful intervention to reduce early stroke recurrence after mild NCIS.

Clinical factors not fully addressed in pivotal clinical trials (or AHA/ASA guidelines) also influenced DAPT prescription in our study. Higher DAPT prescription in large-artery atherosclerosis mild strokes is likely related to results extrapolation from SAMMPRIS (Stenting Versus Aggressive Medical Therapy for Intracranial Arterial Stenosis),[28] CLAIR (Clopidogrel Plus Aspirin Versus Aspirin Alone for Reducing Embolization in Patients With Acute Symptomatic Cerebral or Carotid Artery Stenosis),[29] and a post hoc analysis of CHANCE,[30] which suggest that DAPT is particularly beneficial in symptomatic intracranial atherosclerotic disease. Although these studies refer to a specific large-artery atherosclerosis subgroup (moderate-to-severe intracranial stenosis), and guidelines do not distinguish NCIS subtypes for CHANCE and POINT-related recommendations, it is likely that physicians favored DAPT prescription in a broader group of large-artery atherosclerosis patients based on a higher stroke recurrence risk compared with other stroke subtypes.[1] Similarly, we attribute greater DAPT prescription in patients with high vascular risk profile (ie, diabetes and hyperlipidemia) due to physicians' concern of greater recurrence risk. Contrarily, lower DAPT prescription among small-vessel disease mild strokes is likely related to a perception of lower recurrence risk, and an overinterpretation of studies such as the SPS3 (Secondary Prevention of Small Subcortical Strokes) that showed lack of DAPT benefit for long-term (rather than short-term) secondary prevention in this population.[31]

Premorbid antiplatelet use was the strongest predictor of DAPT prescription in our study. CHANCE and POINT post hoc analyses did not demonstrate differences in DAPT effect between patients who were on premorbid aspirin and those who were not.[2,32] A Korean registry found that ≈60% of physicians added a second antiplatelet agent in NCIS patients who were on aspirin at the time of stroke, and this resulted in ≈50% reduction in vascular events during follow-up.[33] Likewise, a meta-analysis reported that, in NCIS patients on premorbid aspirin, adding or switching to another antiplatelet agent was associated with a decreased incidence of future vascular events, including stroke.[34] Therefore, the more frequent adoption of DAPT in this particular population likely extends beyond the application of CHANCE and POINT findings, and is likely attributable to physicians' intention to add a second antiplatelet agent to mitigate the long-term risk of stroke and vascular events.

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CHANCE and POINT showed that DAPT decrease early stroke recurrence when initiated within 24 hours of symptoms onset, while meta-analysis including less well-design trials suggest that this intervention may be beneficial up to 7 days from symptoms onset.[35,36] Similar to previous reports,[37] nearly two-thirds of our population presented within 24 hours and the vast majority within 7 days. We observed that patients presenting between 1 and 7 days from their last seen well had a ≈14% lower likelihood of being prescribed DAPT. This highlights time-to-presentation as a crucial factor influencing evidence-based DAPT prescription for mild NCIS. However, it also suggests that a notable number of patients receive DAPT even when they present beyond 24 hours from symptoms onset, where the DAPT benefits might not be as significant. Our results underscore the importance of stroke symptoms awareness and early hospital presentation as key factors to increase the use and maximize the benefit of this intervention.

Our study strengths rely in the innovative investigation of the factors that influence DAPT prescription after mild NCIS in a large sample of GWTG-S participating hospitals. However, our study has several limitations. First, unlike CHANCE and POINT population, we did not include high-risk transient ischemic attacks due to the known diagnostic imprecision for this condition,[38] and the lack of reliable data to grade its severity. However, this population should also be targeted for interventions disseminating early DAPT use. Second, we did not consider other antiplatelet combinations (ie, aspirin plus dipyridamole or aspirin plus ticagrelor) for which there is evidence supporting as a valid alternative in mild NCIS patients.[39,40] Third, potential explanations not accounted in our study that may contribute to DAPT underutilization include individual-level factors such as allergy to aspirin or clopidogrel, large infarct size despite low NIHSS, physician's perception of increased bleeding risk, and patient's preferences, which cannot be discerned from registry-based data. Although these individual factors represent expected variations in medical practice rather than nonadherence to treatment guidelines, it is unlikely that these conditions fully explain DAPT underutilization. Finally, our study relies on information collected from Florida GWTG-S participating hospitals, which are typically larger centers with greater experience in stroke care management. Despite our substantial coverage in the state of Florida (>95% of stroke centers in the state), and previous studies showing GWTG-S data is representative of US stroke patients,[41] we cannot entirely rule out incomplete generalizability of our results to other states in the US or other populations.

In summary, DAPT prescription early after a mild NCIS has increased in relation to emerging evidence. However, evidence-based DAPT use remains largely underutilized. In our statewide stroke registry among Floridians, patient- and hospital-related factors, previously linked to the adherence of key stroke care performance measures, also correlated with DAPT prescription after a mild NCIS. Therefore, our study suggests that well-recognized stroke care disparities also influence uptake of evidence-based DAPT prescription. Our study concludes that there is a significant opportunity to implement quality improvement interventions focused on the dissemination of evidence-based DAPT for secondary prevention, and consequently reduce stroke care disparities and the risk of early stroke recurrence in this population.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S4
STROBE checklist

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