What should best medical therapy be for patients having CEA? Should it include clopidogrel?

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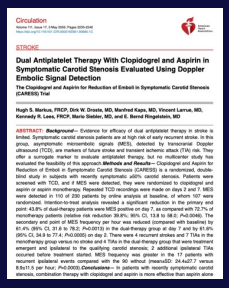
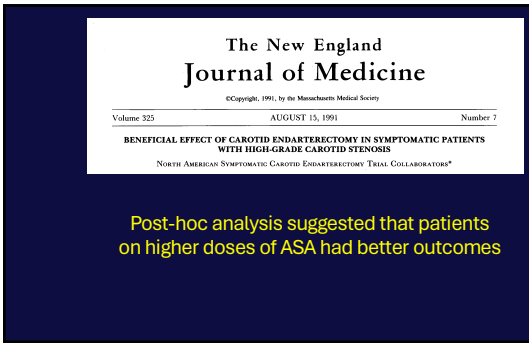


Dual Antiplatelet Therapy With Clopidogrel and Aspirin in Symptomatic Carotid Stenosis Evaluated Using Doppler Embolic Signal Detection

The Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) Trial

CARESS 2005
Symptomatic carotid stenosis

DAPT reduced embolization by 73% compared with monoRx (ASA), as measured by TCD



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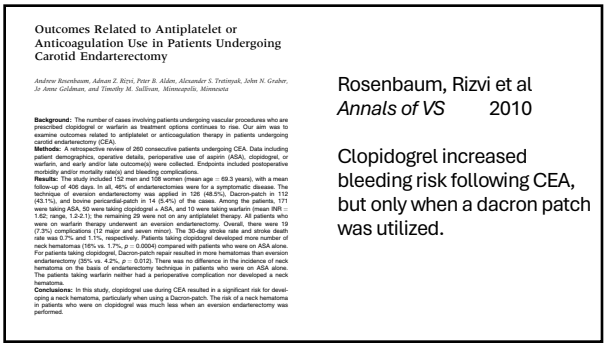
BENEFICIAL EFFECT OF CAROTID ENDARTERECTOMY IN SYMPTOMATIC PATIENTS WITH HIGH-GRADE CAROTID STENOSIS

North American Symptomatic Carotid Endarterectomy Trial Collaborators*

Post-hoc analysis suggested that patients on higher doses of ASA had better outcomes



Outcomes Related to Antiplatelet or Anticoagulation Use in Patients Undergoing Carotid Endarterectomy

Andrew Rosenbaum, Adnan Z. Rizvi, Peter B. Alden, Alexander S. Tretiyak, John N. Graber, Jo Anne Goldman, and Timothy M. Sullivan, Minneapolis, Minnesota

Rosenbaum, Rizvi et al
Annals of VS 2010

Clopidogrel increased bleeding risk following CEA, but only when a dacron patch was utilized.

Clinical trials comparing CEA and CAS
have not utilized equivalent
optimal medical therapy
due to a perceived risk of increased bleeding with
DAPT in CEA

From the Society for Vascular Surgery

Check for updates

Impact of continued clopidogrel use on outcomes of patients undergoing carotid endarterectomy

Jesse Manunga, MD, FACS,[a,b] Christopher Pedersen, MD,[b] Larissa Stanberry, PhD,[b] Akila Pai, MD, MSCR,[c] Nedaa Skeik, MD,[a,b] and Timothy M. Sullivan, MD, FACS,[b] *Minneapolis, MN; and New York, NY*

ABSTRACT

Objective: The aim of this study was to evaluate the use of clopidogrel at the time of carotid endarterectomy (CEA) and its association with postoperative complications.

Methods: Single-institution, retrospective review of a prospective database.

Results: From 2010 to 2017, CEA was performed in 1066 consecutive patients (median age, 73 years; 68% men). The indications for operation included ≥70% asymptomatic stenosis (458; 43%), prior stroke (314; 29%), and transient cerebral or retinal ischemia (294; 28%). At the time of operation, 509 (48%) patients were taking aspirin alone, 441 (41%) were taking clopidogrel (374 in combination with aspirin, 67 as sole therapy), 83 (8%) were on no documented antiplatelet medication, and 33 (3%) were taking warfarin (with therapeutic international normalized ratio). The likelihood of clopidogrel use at the time of operation was higher for patients with a history of symptomatic carotid disease ($P = .002$). Over the study period, clopidogrel use increased from 31.9% in 2010 to 56.8% in 2017, which corresponds to an 11% (95% confidence interval, 6%-15%) increase annually. Postoperative strokes occurred in 15 patients (overall incidence, 1.4%), the majority of which were minor (12/15, 80%). Six strokes occurred in patients taking aspirin alone (6/509; 1.2%), two in patients on clopidogrel and aspirin (2/441; 0.5%), two in patients taking clopidogrel alone (2/67; 2.9%), three in patients on no documented antiplatelet medication (3/83; 3.6%), and two in those taking warfarin (one of which was secondary to a fatal intracranial hemorrhage within 30 days of discharge [2/33; 6.1%]). The 30-day mortality rate was 0.03% (3/1066); the risk for the combined endpoint of any stroke, death, or myocardial infarction (MI) was 2.3% (25/1066), and the risk for major stroke, death, or MI was 1.2%. There was no apparent association between clopidogrel use and the incidence of postoperative bleeding ($P = .59$) or any other postoperative complication (stroke, death, MI, cranial nerve injury; $P = .15$).

Conclusions: Clopidogrel use in our CEA practice has increased over time and has not been associated with an increased risk of postoperative complications, including bleeding. These data suggest that clopidogrel should not be discontinued prior to CEA and should be considered as part of 'optimal medical therapy' in patients undergoing CEA. (J Vasc Surg 2023;78:438-45.)

Manunga, et al
JVS 2023

Study design

- 1066 consecutive patients having CEA 2010-2017
- Retrospective review of a prospective database
- All patients were evaluated with NIH stroke scale pre- and post-operatively

Study design

- Primary endpoints:
  - Postop stroke, MI, death
- Secondary endpoints:
  - Postoperative bleeding
  - Cranial nerve injury

Table III. Carotid artery disease Summary

Summarized by gender

	Overall, N = 1066[1]	Female, N = 364 (34%)[1]	Male, N = 702 (66%)[1]	p-value[2]
Symptomatology				.381
Asymptomatic	458 (43%)	159 (44%)	299 (43%)	
Stroke	294 (28%)	107 (29%)	187 (27%)	
TIA/amaurosis fugax	314 (29%)	98 (27%)	216 (31%)	

57% operated for symptomatic carotid artery stenosis
28% prior CVA
29% TIA / amaurosis fugax

Table II. Coronary Artery Disease Summary

Summarized by clopidogrel use

	Overall, N = 1066[1]	Clopidogrel, N = 441 (41%)[1]	No Clopidogrel, N = 625 (59%)[1]	p-value[2]
CAD Grade				0.002
Grade 1	458 (43%)	165 (37%)	293 (47%)	
Grade 2	294 (28%)	144 (33%)	150 (24%)	
Grade 3	314 (29%)	132 (30%)	182 (29%)	

Table IV. Summary of Outcomes
Summarized by medication group

	Overall, N = 1066[1]	ASA only, N = 509 (48%)[1]	ASA + Clopidogrel, N = 374 (35%)[1]	Clopidogrel only, N = 67 (6.3%)[1]	Warfarin, N = 33 (3.1%)[1]	No Anticoagulants, N = 83 (7.8%)[1]	p-value[2]
Hematoma							0.873
Observed	20 (57%)	9 (60%)	4 (50%)	1 (33%)	3 (75%)	3 (60%)	
Returned to OR	15 (43%)	6 (40%)					
MI	11 (1.0%)	5 (1.0%)					8
Ipsilateral Stroke							5
TIA	9 (38%)	5 (45%)					
Minor	12 (50%)	6 (55%)					
Major	3 (12%)	0 (0%)					
Cranial Nerve Injury							99
Temporary	8 (73%)	6 (67%)					
Permanent	3 (27%)	3 (33%)					
30d - Mortality	3 (0.3%)	0 (0%)	0 (0%)	1 (1.5%)	1 (3.0%)	1 (1.2%)	0.004
MACE	27 (2.5%)	11 (2.2%)	8 (2.1%)	3 (4.5%)	2 (6.1%)	3 (3.6%)	0.270

Major stroke: 0.2%
Minor stroke: 1.1%
CN injury: 1.0%

Death + stroke + MI: 2.5%

The use of DAPT reduced the risk of stroke by half
Reduced the risk of MI, especially in pts with more advanced CAD

The association between Anticoagulation/antiplatelet therapy and outcomes
Based on a univariate model

	RR[1]	95%CI	p.value
MACE, n=27			
ASA only	1.15	(0.50, 2.67)	0.73
Warfarin	0.41	(0.11, 2.59)	0.24
No Anticoagulants	0.69	(0.22, 2.99)	0.56
Hematoma, n=35			
ASA only	1.08	(0.68, 1.69)	0.75
Warfarin	0.65	(0.34, 1.32)	0.21
No Anticoagulants	0.65	(0.36, 1.23)	0.17

No difference in MACE or bleeding based on anticoagulation status

Conclusions

- The use of DAPT did not increase the risk of bleeding or CN injury following CEA
  - Clopidogrel (Rx 30) + 81 mg ASA
  - Begin 7 d prior to CEA, complete P/O, then ASA alone
- Reduced the risk of stroke by half in our series
- Reduced the risk of MI in patients with advanced CAD

Conclusions

- DAPT with ASA and clopidogrel should be considered 'best medical therapy' in patients having CEA
- Future trials comparing CEA and CAS should employ identical adjuvant medical therapies, including DAPT