ACS and Beyond

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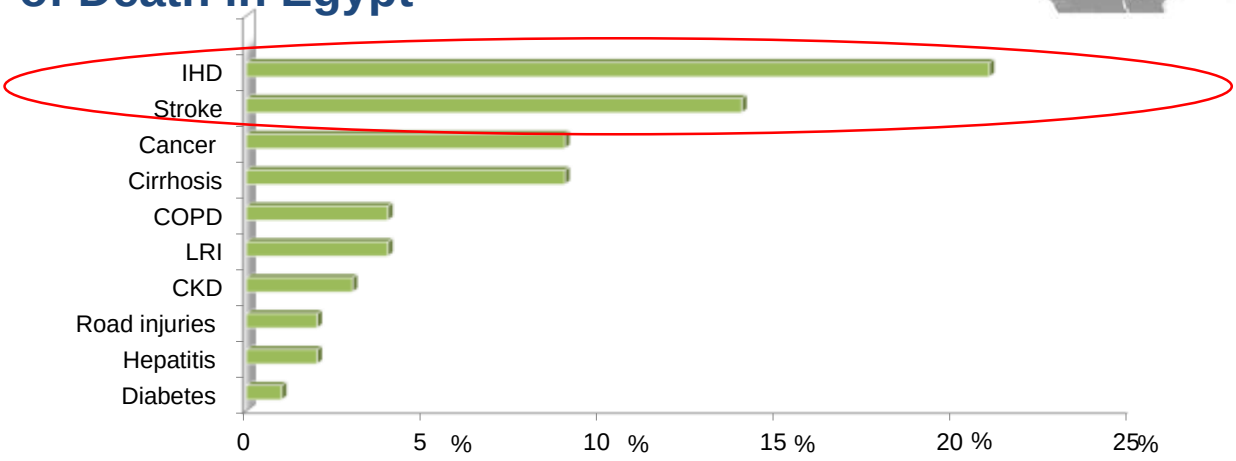
Cairo University

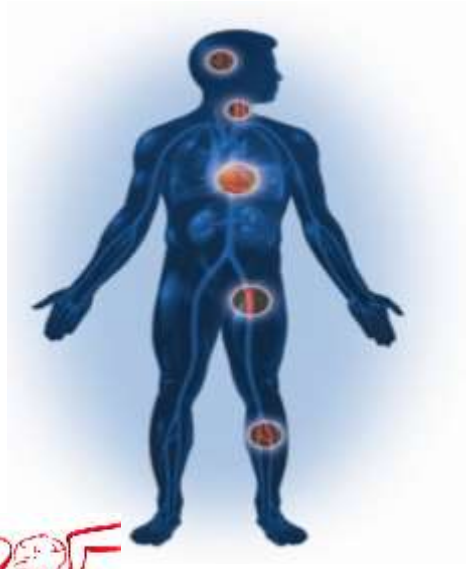
Ischemic Heart Disease and Stroke Represent the First 2 Common Causes of Death in Egypt



IHD: Ischemic heart disease; COPD: chronic obstructive lung disease, LRI: lower respiratory infections, CKD: chronic kidney disease.

Source: GBD Compare (http://v iz.healthmetricsandev aluati on.or g/ g bd-compare/), 2010 available at: http://www.cdc.gov/globalhealth/countries/egypt/pdf/egypt_factsheet.pdf. Accessed on May 24, 2016

IHD, Ischemic Stroke, and PAD are the major clinical manifestations of atherosclerosis



Ischemic Stroke,Or CAD

Ischemic Heart Disease (IHD)

Peripheral Arterial Diseases (PAD)

Circ Res. 2016;118:535-546

REACH Registry

One-Year Cardiovascular Event Rates in Outpatients With Atherothrombosis

Ph. Gabriel Steg, MD
Deepak L. Bhatt, MD
Peter W. F. Wilson, MD
Ralph D'Agostino, Sr, MD

Context Few data document current cardiovascular (CV) event rates in stable patients with atherothrombosis in a community setting. Differential event rates for patients with documented coronary artery disease (CAD), cerebrovascular disease (CVD), or peripheral arterial disease (PAD) or those at risk of these diseases have not been previously evaluated in a single international cohort.

International, prospective cohort, **2003-2004**

68, 236 patients

with either **established atherosclerotic arterial disease**

(CAD, PAD, CVD; n=55 814) or at **least 3 risk factors** for atherothrombosis (n=12 422), enrolled from 5587 physician practices, in 44 countries

REACH: The Reduction of Atherothrombosis for Continued Health

JAMA. 2007;297:1197-1206

REACH Registry inclusion criteria

:

Patients aged ≥45 years

At least 1 of four criteria

1. Documented cerebrovascular disease
   Ischemic stroke or TIA
2. Documented coronary disease
   Angina, MI, angioplasty/ stent/bypass
3. Documented historical or current intermittent claudication associated with ABI <0.9
4. At least 3 atherothrombotic risk factors

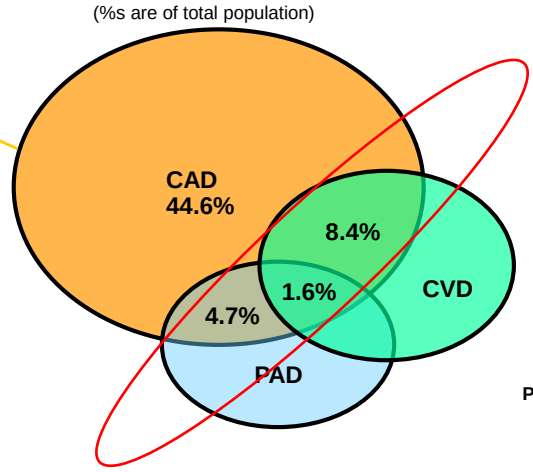
1. Male aged ≥65 years or female aged ≥70 years
2. Current smoking >15 cigarettes/day
3. Type 1 or 2 diabetes
4. Hypercholesterolemia
5. Diabetic nephropathy
6. Hypertension
7. ABI <0.9 in either leg at rest
8. Asymptomatic carotid stenosis ≥70%
9. Presence of at least one carotid plaque

Am Heart J 2006;151(4):786.e1-10.

~25% of patients with CAD have athero-thrombotic disease in other arterial territories

(%s are of total population)

Patients with CAD = 59.3% of the REACH Registry population



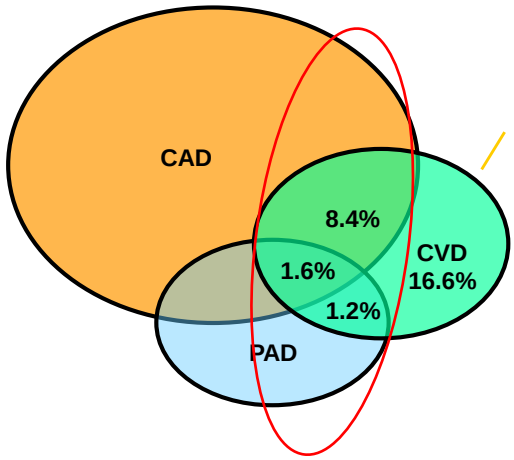
Multiple risk factors only population

CAD=coronary artery disease
PAD=peripheral arterial disease
CVD=cerebrovascular disease

1. Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006;295(2):180-189

~ 40% of patients with cerebrovascular disease have athero-thrombotic disease in other arterial territories

(%s are of total population)



Patients with CVD = **27.8%** of the REACH Registry population

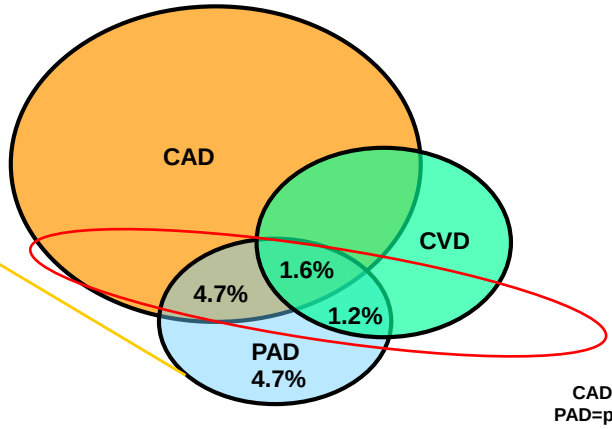
Multiple risk factors only population

CAD=coronary artery disease
PAD=peripheral arterial disease
CVD=cerebrovascular disease

1. Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006;295(2):180-189

~ 60% of patients with PAD have athero-thrombotic disease in other arterial territories

(%s are of total population)



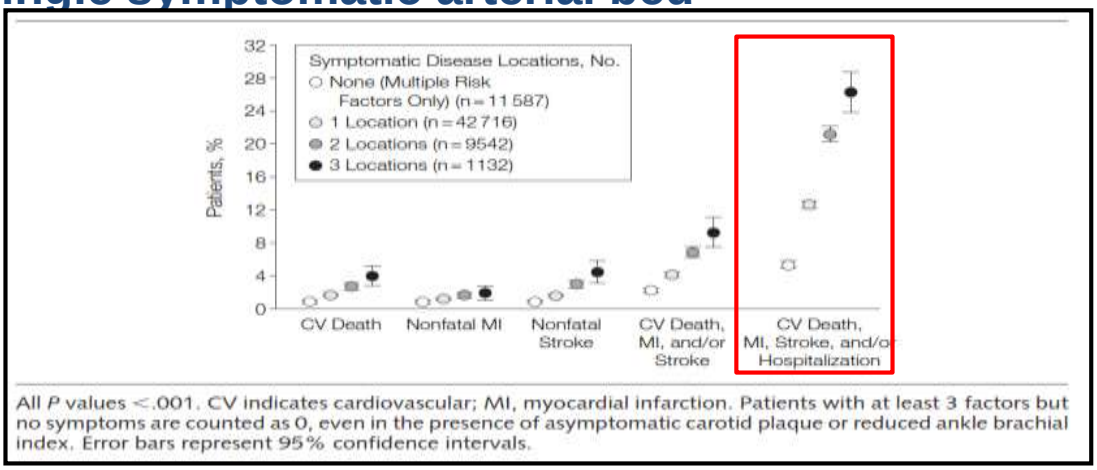
Patients with PAD = **12.2%** of the total REACH Registry population

Multiple risk factors only population

CAD=coronary artery disease
PAD=peripheral arterial disease
CVD=cerebrovascular disease

1. Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006;295(2):180-189.

Major CV event rates were doubled in patients with poly-vascular disease compared with patients with a single symptomatic arterial bed



All *P* values <.001. CV indicates cardiovascular; MI, myocardial infarction. Patients with at least 3 factors but no symptoms are counted as 0, even in the presence of asymptomatic carotid plaque or reduced ankle brachial index. Error bars represent 95% confidence intervals.

One-Year CV Event Rates as a Function of Number of Symptomatic Disease Locations

JAMA. 2007;297:1197-1206

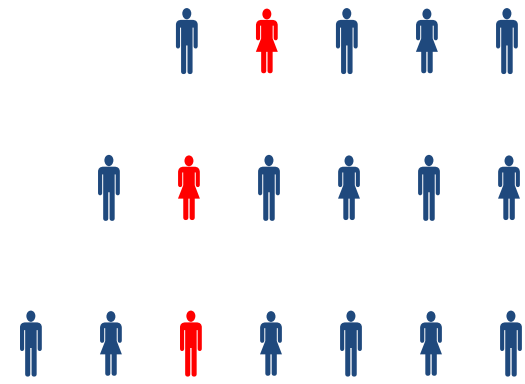
The incidences of CV death, MI, or stroke or of hospitalization for athero-thrombotic event(s) for CAD, CVD, and PAD patients with established disease

Breakdown of event rates

PAD — 21.1% 1 in ~5

CAD — 15.2% 1 in ~6

CVD — 14.5% 1 in ~7

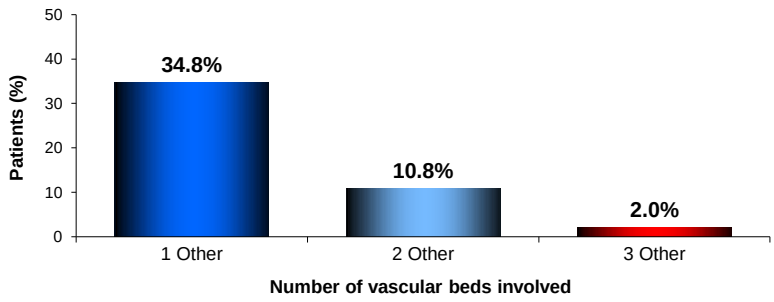


Steg PG *et al*, on behalf of the REACH Registry Investigators. *JAMA* 2007;297(11):1197-1206

What do studies in patients with atherothrombosis show about polyvascular disease?

DETECT: Nearly 50% of Ischemic Stroke Patients Had at Least One Other Form of Vascular Disease

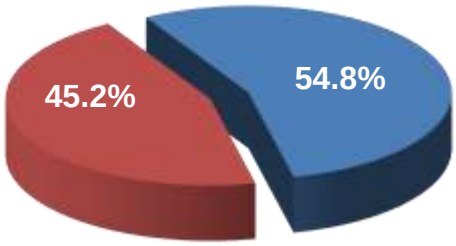
- In the DETECT (Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment) survey, 753 patients admitted for IS were assessed for evidence of disease in other vascular beds*
- 358 of 753 (47.5%) had at least one other manifestation of atherothrombosis



* CAD, aortic atheroma, or PAD, as defined by history and assessment of other vascular beds.

Leys D et al. *Cerebrovasc Dis*. 2006;21:60-66.

SCALA: The Prevalence of PAD in IS Patients



A study of 852 patients with TIA or ischemic stroke found 54.8% patients had a form of PAD. This included:

- ***50.8%*** **of the total population had an ABI ≤0.9**
- ***10.0%*** **of the total population had intermittent claudication**

ABI=Ankle-Brachial Index.
TIA is not a labeled indication in some countries.
Weimar C et al. *J Neurol.* 2007 Aug 3; [Epub ahead of print].

ESC European Society of Cardiology

2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS)

Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries

Endorsed by: the European Stroke Organization (ESO)

The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS)

Authors/Task Force Members: Victor Aboyans* (ESC Chairperson) (France), Jean-Baptiste Ricco*[1] (Co-Chairperson) (France), Marie-Louise E. L. Bartelink (The Netherlands), Martin Björck[1] (Sweden), Marianne Brodmann (Austria), Tina Cohnert[1] (Austria), Jean-Philippe Collet (France), Martin Czerny (Germany),

Aboyans V,Et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS. Eur Heart J. 2017 Aug 26. doi: 10.1093/eurheartj/ehx095.

5. Antithrombotic drugs in peripheral arterial diseases

ESC European Society of Cardiology

Key messages

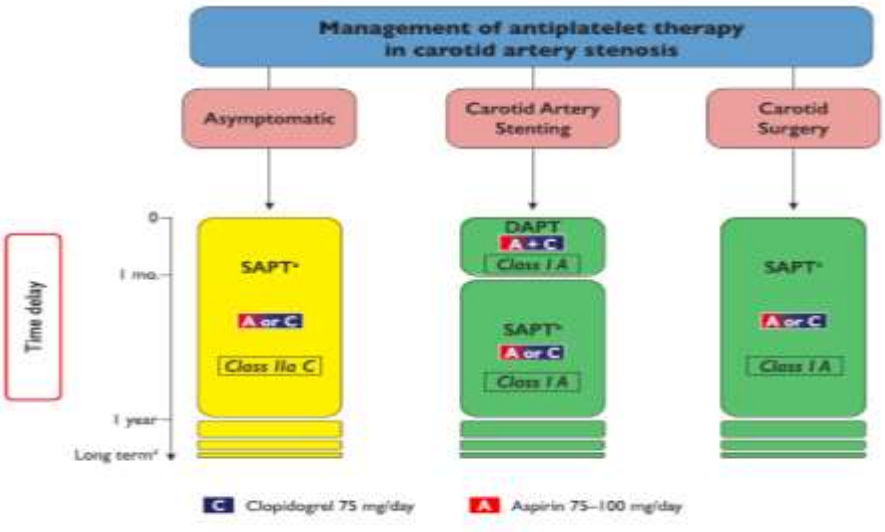
- Antiplatelet therapy is indicated in all patients with carotid artery stenosis irrespective of clinical symptoms and revascularization. Dual antiplatelet therapy (DAPT) should be given for at least 1 month after CAS.
- Single antiplatelet therapy (SAPT) is indicated only if LEAD patients are symptomatic or have undergone revascularization. Clopidogrel is the preferred antiplatelet drug in LEAD patients.
- Chronic anticoagulation therapy is given only if there is a concomitant indication and may be combined with SAPT when there is a recent revascularization procedure.

Antiplatelet therapy is part of BMT for symptomatic PADs (see **chapter 4**). The specific issues about CAD and LEAD are addressed here. The question of DAPT after endovascular therapy in other territories as well as the sensitive issue of PADs patients requiring anticoagulation [e.g. with concomitant atrial fibrillation (AF)] are also addressed.

LEAD: Lower Extremity artery disease

Aboyans V,Et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS. Eur Heart J. 2017 Aug 26. doi: 10.1093/eurheartj/ehx095.

ESC European Society of Cardiology



Aboyans V,Et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS. Eur Heart J. 2017 Aug 26. doi: 10.1093/eurheartj/ehx095.

ESC European Society of Cardiology

6.2.3 Management of vertebral artery disease

Although no prospective RCTs have evaluated different drug therapies in patients with vertebral artery disease, aspirin (or clopidogrel if aspirin is not tolerated) and statins are recommended irrespective of symptoms (see **chapters 4** and **5**). Most patients with asymptomatic vertebral artery disease do not require any revascularization.

Aboyans V,Et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS. Eur Heart J. 2017 Aug 26. doi: 10.1093/eurheartj/ehx095.

Recommendation for stable CAD

ESC European Society of Cardiology

Recommendations on $P2Y_{12}$ inhibitor selection and timing

Recommendations	Class[a]	Level[b]
In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin[c] is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contraindications.[20]	I	B
In patients with ACS undergoing PCI, prasugrel (60 mg loading dose, 10 mg daily dose) on top of aspirin is recommended for $P2Y_{12}$ inhibitor-naive patients with NSTE-ACS or initially conservatively managed STEMI if indication for PCI is established, or in STEMI patients undergoing immediate coronary catheterization[d] unless there is a high risk of	I	B
Clopidogrel (600 mg loading dose, 75 mg daily dose) on top of aspirin is recommended in stable CAD patients undergoing coronary stent implantation and in ACS patients who cannot receive ticagrelor or prasugrel, including those with prior intracranial bleeding or indication for OAC.[20,23,39,40]	I	A
Clopidogrel (300 mg loading dose in patients aged ≤75, 75 mg daily dose) is recommended on top of aspirin in STEMI patients receiving thrombolysis.[31,32]	I	A
Ticagrelor or prasugrel on top of aspirin may be considered instead of clopidogrel in stable CAD patients undergoing PCI, taking into account the ischaemic (e.g. high SYNTAX score, prior stent thrombosis, location and number of implanted stents) and bleeding (e.g. according to PRECISE-DAPT score) risks.	IIb	C
In NSTE-ACS patients in whom coronary anatomy is not known, it is not recommended to administer prasugrel.[33]	III	B

Marco Valgimigli, Et al:2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS, European Heart Journal (2017) 0, 1–48

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor versus Clopidogrel in Symptomatic Peripheral Artery Disease

William R. Hiatt, M.D., F. Gerry R. Fowkes, M.D., Gretchen Heizer, M.S., Jeffrey S. Berger, M.D., Iris Baumgartner, M.D., Peter Held, M.D., Ph.D., Brian G. Katona, Pharm.D., Kenneth W. Mahaffey, M.D., Lars Norgren, M.D., Ph.D., W. Schuyler Jones, M.D., Juuso Blomster, M.D., Marcus Millegård, M.Sc., Craig Reist, Ph.D., and Manesh R. Patel, M.D., for the EUCLID Trial Steering Committee and Investigators*

CONCLUSIONS

In patients with symptomatic peripheral artery disease, ticagrelor was not shown to be superior to clopidogrel for the reduction of cardiovascular events. Major bleeding occurred at similar rates among the patients in the two trial groups. (Funded by AstraZeneca; EUCLID ClinicalTrials.gov number, NCT01732822.)

Jones WS, Baumgartner I, Hiatt WR, et al: Ticagrelor Compared With Clopidogrel in Patients with Prior Lower Extremity Revascularization for Peripheral Artery Disease.Circulation. 2016 Nov 13. pii: CIRCULATIONAHA.116.025880.

2011 AHA/ASA Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack

Table 9. Recommendations for Antithrombotic Therapy for Noncardioembolic Stroke or TIA (Oral Anticoagulant and Antiplatelet Therapies)

Recommendations	Class/Level of Evidence*
For patients with noncardioembolic ischemic stroke or TIA, the use of antiplatelet agents rather than oral anticoagulation is recommended to reduce risk of recurrent stroke and other cardiovascular events *(Class I; Level of Evidence A)*.	Class I; Level A
Aspirin (50 mg/d to 325 mg/d) monotherapy *(Class I; Level of Evidence A)*, the combination of aspirin 25 mg and extended-release dipyridamole 200 mg twice daily *(Class I; Level of Evidence B)*, and clopidogrel 75 mg monotherapy *(Class IIa; Level of Evidence B)* are all acceptable options for initial therapy. The selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, cost, tolerance, and other clinical characteristics.	Class I; Level A; Class I; Level B; Class IIa; Level B
The addition of aspirin to clopidogrel increases risk of hemorrhage and is not recommended for routine secondary prevention after ischemic stroke or TIA *(Class III; Level of Evidence A)*.	Class III; Level A
For patients allergic to aspirin, clopidogrel is reasonable *(Class IIa; Level of Evidence C)*.	Class IIa; Level C
For patients who have an ischemic stroke while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit. Although alternative antiplatelet agents are often considered, no single agent or combination has been studied in patients who have had an event while receiving aspirin *(Class IIb; Level of Evidence C)*.	Class IIb; Level C

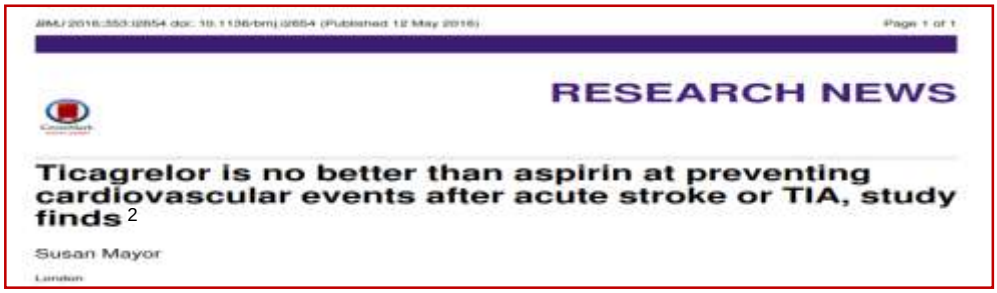
*See Tables 1 and 2 for explanation of class and level of evidence.

AHA: American heart association; ASA: American Stroke Association

Stroke. 2011; 42: 227-276

Newer P2Y12 inhibitors in patients with prior stroke or TIA

pidogrel therapy.[150,151] Prasugrel is contraindicated in patients with prior stroke/transient ischaemic attack (TIA) due to evidence of net harm in this group in TRITON-TIMI 38.[1] In addition, the



RESEARCH NEWS

Ticagrelor is no better than aspirin at preventing cardiovascular events after acute stroke or TIA, study finds[2]

Susan Mayor

London

thebmj

May 2016

1. Eur Heart J. 2016 Jan 14;37(3):267-315
2. BMJ 2016;353:i2654

Conclusion

- **Clopidpgrel is P2Y12 inhibitor of choice in patients received lytic therapy**
- **Clopidpgrel is P2Y12 inhibitor of choice in patients with LEAD[1]**
- **Clopidpgrel is P2Y12 inhibitor of choice in patients with CAS[1]**
- **Clopidpgrel is P2Y12 inhibitor of choice in patients with stable CAD undergoing PCI[2]**
- **Clopidpgrel is P2Y12 inhibitor of choice in patients received triple therapy**
- **Clopidpgrel Has convenient once daily dosing, and Is generally well tolerated**

LEAD: Low extremity arterial disease **CAS : Carotid artery stenting** **CAD : Coronary artery Disease**

1,2:Aboyans V,Et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS. Eur Heart J. 2017 Aug 26. doi: 10.1093/eurheartj/ehx095

2:Marco Valgimigli, Et al:2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS, European Heart Journal (2017) 0, 1–4

Thank you