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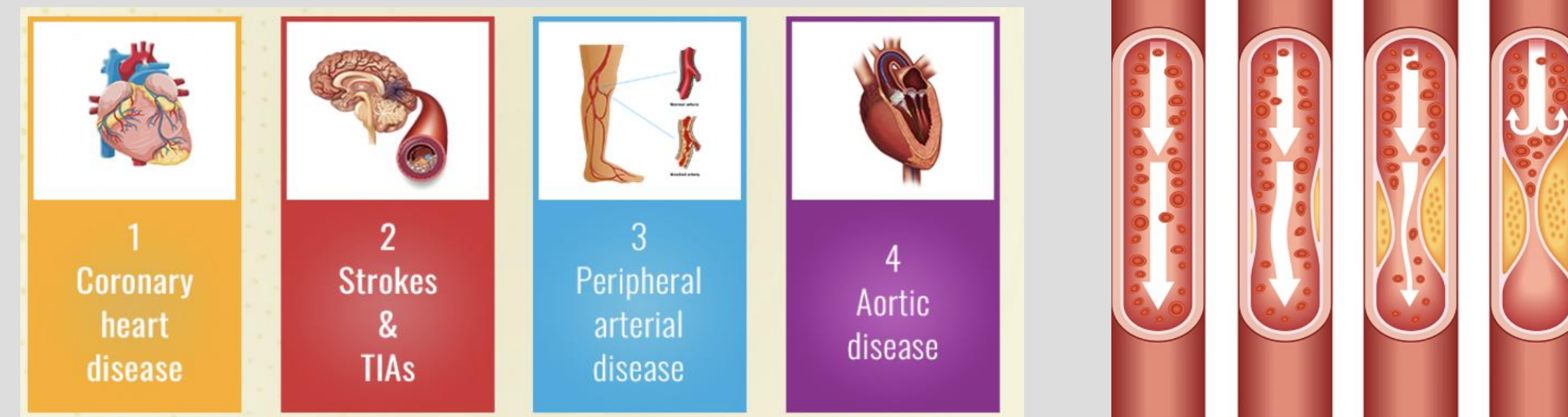
A Comparison of Bleeding Risk in Patients with Cardiovascular Disease Treated with Aspirin versus

Clopidogrel

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Background

Cardiovascular disease is the leading cause of death for men and women in the United States.⁷ There are four main types of CVD:



Coronary artery disease (CAD) is the most prevalent and most common cause of atherosclerosis

Antiplatelet medications remain the cornerstone of medical therapy for primary and secondary atherosclerotic CAD prevention.

Aspirin is prescribed for:

- Individuals with a history of MI or ischemic stroke to prevent a recurrence.
- When a myocardial infarction (MI) is suspected to avoid further infarction.
- Thromboembolism prevention after hip surgeries, transient ischemic attack (TIA) prevention, or adults at a higher risk for atherosclerotic CVD.

Clopidogrel is prescribed for:

- Individuals with a history of MIs, ischemic strokes, and peripheral artery disease.
- Use during a percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS) and stable ischemic heart disease.
- Symptomatic carotid artery stenosis
- Secondary prevention post-coronary artery bypass grafting
- Peripheral artery percutaneous angioplasty in peripheral artery bypass grafting

Introduction

Purpose

To investigate whether aspirin vs. clopidogrel will improve morbidity and mortality in the setting of cardiovascular disease (CVD) and a high bleeding risk to develop clear practice guidelines and improve patient outcomes.

Current guidelines

All patients with acute coronary syndrome should start long-term (>12 months) antiplatelet therapy, with aspirin often being the first-line therapy.⁵

The USPTF recommendation for primary prevention is to take low-dose aspirin (75-100 mg orally once daily) for individuals between the ages of 40 and 59 with a 10% or greater 10-year CVD risk.¹¹

First Line

Aspirin is an effective high-intensity antiplatelet drug that is the first choice in secondary prevention antiplatelet monotherapy in stable patients.¹⁰ However, its potent antithrombotic effects carry a higher risk of bleeding compared to placebo.

Aspirin has been the standard of care in the primary prevention of CVD since the early 2000s, analysis shows that clopidogrel has lower risks of bleeding events.¹

Materials and methods

To evaluate whether aspirin or clopidogrel will decrease morbidity and mortality in patients with CVD and high bleeding risk, the following databases were used: PubMed, NCBI, ScienceDirect, Cochrane Library, and UpToDate. Six research articles were utilized using this search from January to May 2023. Five articles published within the past five years and one older article was used.

Inclusion criteria will be: in adults aged >19yo, English language, systematic review, randomized control trial, and meta-analysis. Exclusion criteria will be ages <19 and studies using clopidogrel and aspirin as dual therapy.

Results

Bleeding

Low-dose aspirin for cardiovascular prophylaxis increased the risk of significant bleeding 2-fold when compared with placebo.¹

A meta-analysis for significant bleeding rates compared five treatments in addition to a placebo and found that clopidogrel had the lowest probability of bleeding (P-score = 0.73) and aspirin with the highest probability of bleeding (P-score = 0.48).¹

GI Bleeding

The most common type of bleeding was GI.

One randomized controlled trial showed that the risk of GI bleeding was higher in aspirin compared to clopidogrel: 1.08% vs 0.74%.³

Intracranial Bleeding

When they compared intracranial bleeding, they found that clopidogrel had a lower risk than aspirin.¹

Fatal Bleeding

Fatal bleeding was also lower in the clopidogrel group than in aspirin

	Aspirin	Clopidogrel
Total enrolled	9586	9599
Any bleeding	9.28% (890)	9.27% (890)
Any fatal bleeding	0.28% (27)	0.24% (23)
All GI bleeding	2.66% (255)	1.99% (191)
Intracranial bleeding	0.49% (47)	0.35% (34)
Non-GI, non-intracranial bleeding	0.42% (40)	0.57% (55)

Table 1. Comparing bleeding risk in aspirin vs. clopidogrel³

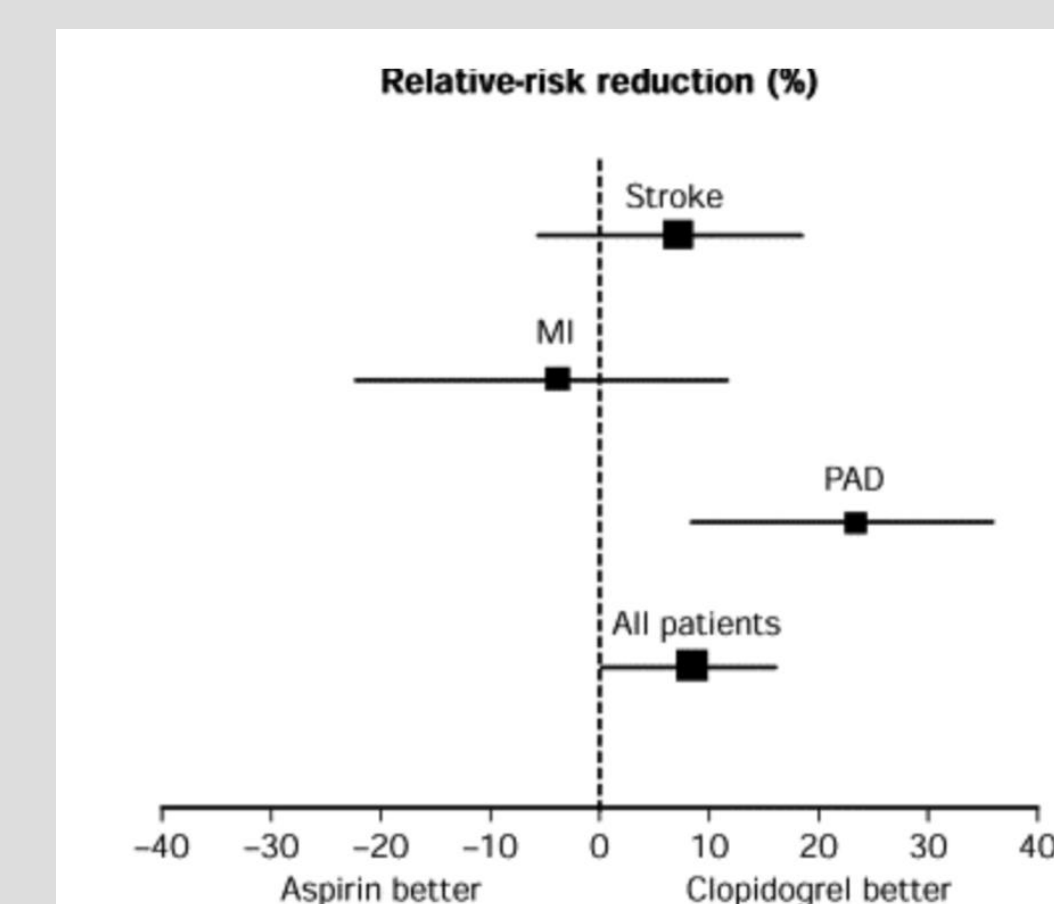


Table 2. Relative-risk reduction in aspirin vs clopidogrel¹²

Morbidity and Mortality

One systematic review and meta-analysis found that clopidogrel reduced the risk of death, MI, and ischemic stroke.³

A separate systematic review and meta-analysis found lower risks of CVD and recurrent ischemic stroke for clopidogrel monotherapy than aspirin.⁴

There was no change in mortality between the two groups.⁴

CAPRIE Study Evaluated the safety and efficacy of aspirin vs. clopidogrel in reducing the primary outcomes of ischemic strokes, MI, or vascular death.

Long term (>12 months), clopidogrel had better efficacy when compared to aspirin for reducing vascular events, ischemic stroke, and acute MI among most groups.¹²

Aspirin was more effective in the subgroup of prior MI patients, as seen in Table 2.¹²

Individuals on clopidogrel had a lower risk of recurrent ischemic stroke after one year; however, the risk of death was similar between the two drugs.³

In the CAPRIE study, clopidogrel was moderately more effective than aspirin in reducing cardiovascular events.¹²

HOST-EXAM Assessed the safety and efficacy of aspirin and clopidogrel among patients who had completed the required duration of DAPT after a PCI.⁵

Findings showed that all-cause death, non-fatal MI, stroke (ischemic), and readmission for clopidogrel vs. aspirin, was 5.7% vs. 7.7%.

Conclusions

Clopidogrel Over Aspirin?

Studies comparing clopidogrel and aspirin have shown that clopidogrel has a lower risk of bleeding as well as reduced rates of morbidity and mortality in specific populations.

Individuals who completed DAPT after a PCI were the only identified population with reduced morbidity and mortality with clopidogrel.⁵

Marginal Difference

The data between the two drugs is often marginal; therefore, more studies should be conducted to determine which population may benefit more.

Some studies demonstrated no difference in morbidity and mortality between aspirin and clopidogrel.⁴

The absolute increase in the incidence of major bleeding with aspirin vs. clopidogrel is relatively small.

See also: aspirin side effects in more detail.		See also: Plavix side effects in more detail.	
Pricing and Coupons			
* Prices are without insurance			
Quantity	100 tablet	Quantity	90 tablet
Dosage	325 mg	Dosage	75 mg
Per Unit*	\$0.10	Per Unit*	\$8.37
Cost*	\$10.33	Cost*	\$753.37

Future Studies

Although clopidogrel is often used as an alternative for individuals intolerant to aspirin, few head-to-head and placebo studies have been done to compare the two. Further assessment of safety and efficacy of these drugs using large-scale population studies would also be beneficial.

Longitudinal data and exceptional studies comparing the two drugs on morbidity and mortality must be compared to identify additional populations.⁴

Current and future research will create advances in antiplatelet therapy guidelines that will allow healthcare providers to improve clinical outcomes and cost of care.

Future Guidelines

Management of patients who experience bleeding while on antiplatelet therapy poses a dilemma. Providers must decide when it is safe to restart antiplatelet therapy, whether to continue with the same drug, try an alternative, or discontinue antiplatelet therapy altogether. Guidelines should be created regarding treatment options for patients with a bleeding event while on antiplatelet therapy.

Final Thoughts

When instituting antiplatelet therapy, studies suggest that clopidogrel is an effective antiplatelet agent that should be evaluated per patient needs and risk factors to establish benefits in cardiovascular outcomes, bleeding, and morbidity and mortality.

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