

Outcomes in Patients Receiving Dual Antiplatelet Therapy in Combination with Direct Oral Anticoagulants: A Meta-analysis

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Background

- The increasing prevalence of atherosclerotic cardiovascular disease (ASCVD), atrial fibrillation (AF), venous thromboembolism (VTE) and arterial thrombosis (AT) creates frequent scenarios where these pathologies overlap clinically and therapeutically, often requiring a combination of dual antiplatelet therapy (DAPT) and oral anticoagulation (OA) strategies.
- We aimed to conduct a meta-analysis to explore the cardiovascular, thrombosis and bleeding outcomes in patients receiving DAPT and DOAC therapy (Triple therapy)

Methods

- We conducted a literature search of studies exploring the use of DAPT in combination with DOAC therapy with focus on bleeding and thrombosis outcomes including myocardial infarction (MI), stroke, stent thrombosis, limb thrombosis and VTE.
- We used Ovid, Scopus, PubMed, Medline, and EBSCO databases starting from January 2010 to March 2020
- We conducted the literature search using the following combination of terms: (Aspirin AND Clopidogrel OR Prasugrel OR Ticagrelor) AND (Apixaban OR Rivaroxaban OR Edoxaban OR Dabigatran OR Betrixaban).

Results

- A total of 4857 articles. Pre-clinical trials, animal studies, guidelines, review articles, meta-analysis, case reports, editorials, letters and duplicates were discarded.
- A total of 9 studies (**Table 1**), including RCTs and observational studies were included.
- Outcomes collected included composite CV outcomes (CV death, MI, stroke), composite bleeding, major and minor bleeding, and all-cause mortality.
- In patients on triple therapy, the pooled composite CV outcomes weight event average was 3.18 (CI 95% 2.98 – 3.37), composite bleeding was 1.24 (CI 95% 0.83 – 1.65), major bleeding was 0.76 (CI 95% 0.66 – 0.85), and all-cause mortality was 2.47 (CI 95% 2.25 – 2.69).

Conclusions

- Triple therapy scenario is often encountered in clinical practice. Preliminary results of our analysis shows that triple therapy is not innocuous.
- Further comparative meta-analysis of triple therapy versus DAPT is required to assess CV, thrombotic and bleeding outcomes.

Study	Study Type	Year	Number of Patients	Intervention	Events (Outcomes)
Gibson et al	RCT post-hoc analysis	2013	9,631	Patients with ACS +/- PCI receiving DAPT + Rivaroxaban 2.5mg vs DAPT + Rivaroxaban 5 mg vs DAPT + Placebo	Stent thrombosis
Oldgren et al	RCT	2011	1,861	Patients with ACS +/- PCI receiving DAPT + Dabigatran (dose 50, 75, 110, 150mg) vs DAPT + placebo	Primary: Composite bleeding Secondary: Composite of CV mortality, non-fatal myocardial infarction, non-hemorrhagic stroke
Hess et al	RCT post-hoc analysis	2015	7,364	Patients with ACS +/- PCI receiving DAPT + Apixaban vs ASA + Apixaban vs DAPT + Placebo vs ASA + placebo	Primary: (Efficacy) Composite of CV mortality, myocardial infarction or ischemic stroke, (safety) major bleeding Secondary: (Efficacy) All-cause mortality, (safety) Major or minor bleeding
Mega et al	RCT	2012	15,526	Patients with ACS +/- PCI receiving Rivaroxaban 2.5 mg vs 5mg vs Placebo plus aspirin or DAPT	Primary: (efficacy): composite of CV death, myocardial infarction, or stroke, (safety) major bleeding Secondary: (efficacy): death from any cause, myocardial infarction, or stroke.
Russo et al	Prospective observational	2019	350	Patients with PCI receiving DAPT + Dabigatran vs DAPT+warfarin	Primary: (Safety): Major bleeding, (efficacy) composite ischemic stroke, systemic embolism or myocardial infarction Secondary: (Efficacy): CV hospitalization
Sotomi et al	Prospective longitudinal	2019	2,216	Nonvalvular A.fib patients on DOAC. Compare DOAC vs DOAC + SAPT vs DOAC + DAPT	Primary: (safety): Any bleeding, (safety) major bleeding Secondary: (efficiency): All-cause mortality, myocardial infarction, stroke
Casamira et al	Retrospective longitudinal	2019	187	A.fib patients with PCI who are on DOAC + DAPT vs Warfarin + DAPT	Primary: (efficacy): Major acute cardiac events, (safety): Major bleeding Secondary: Composite of Cardiovascular death, myocardial infarction, stroke, stent thrombosis and major bleeding events
Romero et al	Retrospective cross-sectional cohort	2018	367	Patients discharged on DOAC + ASA vs DOAC + P2Y12 Inhibitor vs DOAC + DAPT	Primary: 6-month hospital readmission Secondary: Bleeding All-cause mortality
Sindet et al	Retrospective longitudinal	2018	3,222	A.fib patients with hospitalization for MI, PCI or both on DOAC or VKA plus SAPT or DAPT	Primary: Ischemic stroke and myocardial infarction Secondary: All-cause mortality and bleeding

Table 1: Selected Articles for Meta-Analysis