EFFICACY AND SAFETY OF ANTITHROMBOTIC THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION WHO UNDERWENT PERCUTANEOUS CORONARY INTERVENTIONS

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Abstract: *Reducing cardiovascular risk by decreasing cardiovascular morbidity and mortality is considered one of the main objectives of modern cardiology practice. Oral anticoagulants are the basis for preventing cardioembolic stroke in patients with atrial fibrillation, a condition that often coexists with coronary heart disease. According to statistics, approximately a quarter of patients with atrial fibrillation undergo percutaneous coronary intervention at some point in their lives due to stable angina or acute coronary syndrome. This scenario presents significant challenges related to the use of multicomponent antithrombotic therapy. Antithrombotic therapy in patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI) requires a delicate balance between preventing thromboembolic events and minimizing bleeding complications. This study evaluates the efficacy and safety of antithrombotic strategies, including dual antithrombotic therapy (DAT) and triple antithrombotic therapy (TAT), in this high-risk population. This article reviews the key clinical data and recommendations for the optimal use of combined antithrombotic therapy in patients following percutaneous coronary intervention.*

Key words: *atrial fibrillation, coronary stenting, oral anticoagulant, oral antiplatelet, percutaneous coronary intervention.*

Atrial fibrillation (AF) is the most common heart rhythm disorder in the general population. A 2018 statistical update from the American Heart Association (AHA) reports estimates of AF prevalence in 2010 ranging from ≈2.7 to 6.1 million in the United States and 8.8 million (95% confidence interval [CI]: 6.5 to 12.3 million) in Europe.[1] Most patients with atrial fibrillation (AF) and risk factors for stroke require oral anticoagulation (OAC) to prevent cerebrovascular or systemic embolism.[2] AF increases the risk of thromboembolic complications, including

stroke and extracranial systemic embolic events, which call for therapeutic prophylaxis with oral anticoagulation (OAC) [3] The CHA_2DS_2-VASc scale is widely used to stratify the risk of thromboembolic complications in patients with AF: with a score of 1 point (except for female patients who do not have additional risk factors), the advisability of preventing thromboembolic complications is not so obvious, but it is recommended to consider the possibility of prescribing antithrombotic drugs; with a score of 2 points for men and more than 2 points for women, it is necessary to prescribe oral anticoagulants (OAC) to prevent the risk of thromboembolic complications, in particular ischemic stroke. [4]

UP to 40% of patients with AF also have coronary artery disease (CAD), many of whom require revascularization. [5] some of the patients whom requires revascularization using percutaneous coronary intervention (PCI) and stent implantation. In patients who are prescribed OAC, antiplatelet drugs must be added to the therapy during PCI, which is associated with a high risk of hemorrhagic complications. Such patients need dual antiplatelet therapy (DAPT) to prevent the risk of stent thrombosis and additional thrombotic ischemic events. [6]

Challenges in Antithrombotic Therapy

Patients with AF undergoing PCI often require a combination of anticoagulants and antiplatelet agents. The traditional triple antithrombotic therapy (TAT), consisting of an oral anticoagulant, aspirin, and a P2Y inhibitor, is effective in reducing thromboembolic and ischemic events. However, this regimen significantly increases the risk of bleeding complications, which can outweigh the benefits in certain patients. Recent studies and clinical guidelines emphasize the use of dual antithrombotic therapy (DAT), which eliminates aspirin, aiming to minimize bleeding risks while maintaining adequate protection against thromboembolic events.

In 2012, the results of the first randomized WOEST study (573 patients) were published, which compared two therapy regimens - triple (warfarin + clopidogrel + aspirin) and dual (warfarin + clopidogrel) antiplatelet therapy [9,13]. The study included patients with AF (70%), mechanical heart valves (10%), pulmonary embolism (PE), left ventricular thrombosis, who underwent PCI on a planned or emergency basis for acute coronary syndrome (ACS) (patients with ACS made up 25-30% of the total number of patients included in the study). The results of the study demonstrated the advantage of dual therapy with warfarin and clopidogrel over triple

therapy in terms of achieving the primary endpoint - hemorrhagic events (19.5% versus 44.9%; odds ratio (OR) 0.36; 95% confidence interval (CI) 0.26-0.50; $p < 0.001$) [7,12]. Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor should be given to all patients during the peri-PCI period (during inpatient stay, until time of discharge, up to 1 week after PCI, at the discretion of the treating physician), after which the default strategy is to stop aspirin and continue treatment with a P2Y12 inhibitor, preferably clopidogrel.

The combination of OAC and DAPT, a regimen also known as triple antithrombotic therapy (TAT), is theoretically required to decrease both the risk of thromboembolism due to AF and the risk of thrombotic events due to coronary stents in patients with underlying CAD. However, TAT markedly increases the risk of major and fatal bleeding. [8,11] When warfarin is prescribed as part of triple therapy, stricter INR limits are recommended: several small prospective studies have shown a significant reduction in the percentage of major bleeding when a target INR of 2.0-2.5 is achieved compared with an INR of 2.0-3.0. [9,10]

Management of AF Patients Undergoing PCI

A patient undergoing PCI often requires long-term anticoagulant therapy, with atrial fibrillation (AF) being the most common reason. It has been proven that the combination of various forms of coronary heart disease with AF increases significantly with age. The prevalence of coronary heart disease in patients with AF, as indicated in studies, can range from 17% to 50%, and in elderly patients, it may be as high as 82%. As part of a general periprocedural bleeding avoidance strategy, procedures should be carried out with radial access. However, these therapies carry a significant risk of bleeding, especially when used together as part of triple antithrombotic therapy (TAT). Identifying the appropriate regimen and duration of therapy for each patient depends on several factors, including:

- Stroke risk (e.g., CHA_2DS_2-VASc score)
- Bleeding risk (e.g., HAS-BLED score)
- Type of stent used (bare-metal vs. drug-eluting)
- Clinical presentation (e.g., stable CAD vs. acute coronary syndrome)

DAT combines an OAC (preferably a NOAC) with a single antiplatelet agent (typically a $P2Y_{12}$ inhibitor like clopidogrel). Evidence from trials such as PIONEER AF-PCI, RE-DUAL PCI, and AUGUSTUS has demonstrated that DAT is associated

with a significant reduction in bleeding complications without compromising ischemic protection. This makes DAT the preferred long-term strategy for most patients. Default DAPT durations in these settings are 6 and 12 months, respectively, but these durations are flexible depending on the individual risk of ischemia and bleeding[10]

Safety Considerations

Bleeding remains the most significant adverse event associated with antithrombotic therapy. Major bleeding can lead to increased mortality, prolonged hospitalization, and reduced quality of life. The use of NOACs, such as rivaroxaban, apixaban, or dabigatran, has been associated with lower bleeding risks compared to vitamin K antagonists (VKAs) like warfarin.

Additionally, eliminating aspirin from TAT to form DAT has been shown to significantly reduce major and minor bleeding events without compromising efficacy.

Recent guidelines from the European Society of Cardiology (ESC) and the American Heart Association (AHA) emphasize individualized therapy based on patient-specific risks. Key recommendations include:

1. Risk Stratification:
   - Assess stroke risk using the CHA_2DS_2-VASc score.
   - Evaluate bleeding risk using the HAS-BLED score.
2. Antithrombotic Regimen:
   - Use TAT only in the short term (1–4 weeks) for patients at high ischemic risk.
   - Transition to DAT with a NOAC and clopidogrel as the long-term regimen for most patients.
3. Choice of NOAC:
   - Use reduced-dose NOAC regimens as studied in clinical trials (e.g., rivaroxaban 15 mg daily or dabigatran 110 mg twice daily).
4. Duration of Therapy:
   - Tailor the duration of antiplatelet therapy based on bleeding and ischemic risk. For patients with stable CAD, aspirin is often discontinued after the initial period.

Conclusion: The management of antithrombotic therapy in patients with AF undergoing PCI requires a careful balance between reducing thrombotic risk and minimizing bleeding complications. Evidence supports the use of DAT as a safer and equally effective alternative to TAT in most patients, with NOACs playing a central

role. Future research should focus on further personalizing antithrombotic regimens to optimize outcomes for individual patients.

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