

COMPARISON OF DUAL VERSUS TRIPLE ANTITHROMBOTIC THERAPY IN ATRIAL FIBRILLATION WITH CORONARY ARTERY DISEASE: A RETROSPECTIVE STUDY

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ABSTRACT

Background: Patients with atrial fibrillation (AF) and coronary artery disease (CAD) often require combined antithrombotic therapy, but the optimal balance between prevention of thromboembolic and ischemic events and reduction of bleeding risk remains uncertain. **Objective:** This study compared clinical outcomes associated with dual versus triple antithrombotic therapy in this high-risk population. **Methods:** This retrospective comparative cohort study was conducted at Army Cardiac Hospital Lahore from January 06, 2026 to August 05, 2026, included 238 patients with AF and CAD, of whom 118 received dual antithrombotic therapy and 120 received triple antithrombotic therapy. Clinical outcomes including thromboembolic events, myocardial infarction, stent thrombosis, major bleeding, clinically relevant non-major bleeding, and mortality were evaluated and compared between groups. **Results:** Thromboembolic events were observed in 10.2% of patients receiving dual therapy and 8.3% receiving triple therapy ($p=0.62$), while rates of myocardial infarction, stent thrombosis, and major adverse cardiovascular events were also comparable between groups. Major bleeding occurred significantly less frequently in the dual therapy group compared with the triple therapy group (7.6% vs 17.5%, $p=0.03$). Clinically relevant non-major bleeding was also lower with dual therapy (14.4% vs 25.0%, $p=0.04$). Multivariable analysis identified triple therapy and elevated HAS-BLED score as independent predictors of major bleeding. **Conclusion:** Dual antithrombotic therapy demonstrated comparable efficacy to triple therapy for prevention of thromboembolic and ischemic events while significantly reducing bleeding complications.

KEYWORDS: dual antithrombotic therapy, triple antithrombotic therapy, high-risk population, Atrial Fibrillation, Coronary Artery Disease

INTRODUCTION

Atrial fibrillation (AF) is the most frequent sustained cardiac arrhythmia in clinical practice and is linked with a significantly high risk of thromboembolic events, especially ischemic stroke and systemic embolism [1]. Meanwhile, coronary artery disease (CAD) is among the most important causes of morbidity and mortality in the world. AF and CAD frequently co-occur, especially in patients of advanced age, with multiple cardiovascular comorbidities, and poses a considerable therapeutic dilemma, as treatment demands a compromise between prevention of thromboembolic, coronary ischemic and bleeding risks [2]. Oral anticoagulation is usually used to prevent strokes in patients with atrial fibrillation, whereas antiplatelet therapy is used to prevent stent thrombosis and repeat ischemic events in patients with coronary artery disease, especially in the post-percutaneous coronary intervention (PCI) or acute coronary syndrome (ACS) settings [3]. In the past, the combination of these overlapping signs resulted in triple antithrombotic therapy, which is oral anticoagulation and dual antiplatelet therapy, typically aspirin and a P2Y₁₂ inhibitor. This method has a wide range of antithrombotic protection, but at the cost of significantly elevated risk of major bleeding, leading to concerns about its safety [4].

Over the past few years, dual antithrombotic therapy, which is generally oral anticoagulation and one antiplatelet agent, has become an option that may be safer than triple therapy [5]. Several large clinical trials have indicated that dual therapy can substantially decrease the occurrence of bleeding complications without a significant increment in thrombotic or ischemic events [6]. These results have questioned the classical paradigms of treatment and brought about a shift in the recommendations of international guidelines towards shorter periods of triple therapy, or an immediate shift to dual therapy in select patients [7]. Although there has been a changing body of evidence, there has been controversy over the best approach to antithrombotic in patients with AF and CAD, especially those at high risk of ischemia, in complex PCI, or in patients with recent acute coronary syndrome. Although dual therapy can minimize bleeding, some questions about the possibility of decreased antiplatelet intensity to promote the risk of myocardial

infarction, stent thrombosis, or re-occurring coronary events in certain patient groups remain [8]. On the other hand, longer triple therapy could provide more ischemic protection at the cost of extremely increased hemorrhagic complications. In this way, the issue of dual versus triple antithrombotic therapy is a highly controversial question of clinical uncertainty [9].

This decision has become even more complicated as the use of direct oral anticoagulants (DOACs) has become widespread, and the risks-benefit considerations have changed compared to vitamin K antagonists in the previous treatment plans. Recent research comparing regimens of DOACs has yielded valuable data, but variations in patient cohorts, periods of treatment, and outcome measures have led to continuing controversy over comparative efficacy of dual versus triple therapy [10]. A major factor to consider in this therapeutic dilemma is that patients with AF and CAD have competing risks. Individuals at a high thromboembolic risk might need to receive powerful anticoagulant to prevent stroke and patients receiving PCI might need to receive antiplatelet coverage against stent thrombosis, especially in the early post-procedural period [11]. Concurrently, most of these patients are older adults and have comorbidities like chronic kidney disease, diabetes, hypertension, and a history of bleeding, which all put them at risk of bleeding. This ischemic-bleeding overlap is what complicates individualized antithrombotic therapy especially [12]. Large, randomized studies, including those that analyze DOAC-based dual therapies, have typically demonstrated a decrease in clinically significant bleeding relative to triple therapy, with no difference in the major adverse cardiovascular event rate [13]. Nevertheless, there are still some questions of whether such outcomes can be completely generalized to all patient populations, especially high thrombotic burden and complicated coronary anatomy. Clinicians still prefer short term triple therapy in some high-risk populations, although others would prefer de-escalation to dual therapy early in an attempt to reduce morbidity related to bleeding [14]. Such variations indicate the continued ambiguity in practice. The adverse event of bleeding is not trivial in this population. The possibility of major bleeding can lead to hospitalization, transfusion, antithrombotic therapy discontinuation, and death. Significantly, in some cases, bleeding can ironically put patients at risk of ischemic diseases by forcing them to prematurely abandon antithrombotic drugs [15].

Objective

This study compared clinical outcomes associated with dual versus triple antithrombotic therapy in this high-risk population.

METHODOLOGY

This was a retrospective comparative cohort study conducted at Army Cardiac Hospital Lahore from January 06, 2026 to August 05, 2026. A total of 238 patients were included. Non-probability consecutive sampling was used to include eligible patients meeting the study criteria. Included were adult patients who had documented atrial fibrillation and concomitant coronary artery disease at the age of 18 years and were on either dual antithrombotic therapy (oral anticoagulant plus single antiplatelet agent) or triple antithrombotic therapy (oral anticoagulant plus dual antiplatelet therapy). Patients who received follow up records and were treated after suffering percutaneous coronary intervention or acute coronary syndrome were included in the analysis. Patients who had valvular atrial fibrillation, active malignancy, severe hepatic illness, known bleeding disorder, incomplete medical record and less than the predetermined study period were excluded. Patients that had undergone other non-standard antithrombotic regimens were also excluded.

Data Collection

Medical records of eligible patients were reviewed retrospectively after institutional permission. Demographic and clinical characteristics such as age, gender, hypertension, diabetes mellitus, chronic kidney disease, previous stroke, CHA₂DS-VASc score, HAS-BLED score, need of coronary intervention, and antithrombotic regimen type were noted as baseline demographic and clinical. The patients were divided into two groups depending on the treatment they were getting: dual therapy group and triple therapy group. They were followed-up on efficacy and safety outcomes, such as thromboembolic events, myocardial infarction, stent thrombosis, major bleeding, clinically relevant non-major bleeding, all-cause mortality, and hospital readmissions. Clinical records, follow-up visits, and hospitalizations were used to identify outcome events. The key efficacy outcomes were thromboembolic events and major adverse cardiovascular events. Major bleeding was the main safety outcome. Clinically relevant non-major bleeding, all-cause mortality, and treatment-related hospital readmissions were also clinically relevant outcomes.

Data Analysis

Data were entered and analyzed using SPSS version 26.0. Quantitative variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Comparison between dual and triple therapy groups was performed using independent sample t-test for continuous variables and Chi-square or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

Data were collected from 238 patients, mean age was similar (69.1 ± 8.5 vs 69.7 ± 8.9 years), and males constituted the majority in both groups (64.4% vs 66.7%). The prevalence of hypertension (69.5% vs 72.5%), diabetes mellitus (40.7% vs 42.5%), chronic kidney disease (17.8% vs 20.0%), and prior stroke (13.6% vs 15.0%) was comparable. Mean CHA₂DS₂-VASc (3.8 vs 3.9) and HAS-BLED scores (2.4 vs 2.5) were also similar. Most patients underwent PCI (77.1% vs 78.3%), while ACS presentation occurred in 44.1% and 45.8% of patients, respectively.

Table 1. Baseline Demographic and Clinical Characteristics (n=238)

Variable	Dual Therapy (n=118)	Triple Therapy (n=120)
Age (years), mean ± SD	69.1 ± 8.5	69.7 ± 8.9
Male sex, n (%)	76 (64.4)	80 (66.7)
Hypertension, n (%)	82 (69.5)	87 (72.5)
Diabetes mellitus, n (%)	48 (40.7)	51 (42.5)
Chronic kidney disease, n (%)	21 (17.8)	24 (20.0)
Prior stroke, n (%)	16 (13.6)	18 (15.0)
CHA ₂ DS ₂ -VASc score	3.8 ± 1.2	3.9 ± 1.3
HAS-BLED score	2.4 ± 0.9	2.5 ± 1.0
PCI indication, n (%)	91 (77.1)	94 (78.3)
ACS presentation, n (%)	52 (44.1)	55 (45.8)

Thromboembolic events occurred in 10.2% of patients receiving dual therapy and 8.3% receiving triple therapy (p=0.62). Myocardial infarction (5.9% vs 5.0%), stent thrombosis (2.5% vs 3.3%), and major adverse cardiovascular events (11.9% vs 13.3%) were also comparable (p>0.05). Likewise, all-cause mortality (6.8% vs 8.3%) and hospital readmissions (12.7% vs 15.0%).

Table 2. Efficacy Outcomes Comparison

Outcome	Dual Therapy (n=118)	Triple Therapy (n=120)	p-value
Thromboembolic events, n (%)	12 (10.2)	10 (8.3)	0.62
Myocardial infarction, n (%)	7 (5.9)	6 (5.0)	0.78
Stent thrombosis, n (%)	3 (2.5)	4 (3.3)	0.71
Major adverse cardiovascular events, n (%)	14 (11.9)	16 (13.3)	0.74
All-cause mortality, n (%)	8 (6.8)	10 (8.3)	0.66
Hospital readmissions, n (%)	15 (12.7)	18 (15.0)	0.61

Major bleeding occurred less frequently in the dual therapy group (7.6% vs 17.5%, p=0.03), while clinically relevant non-major bleeding was also lower (14.4% vs 25.0%, p=0.04). Any bleeding event occurred in 22.0% of dual therapy patients compared with 42.5% in the triple therapy group (p=0.001). Bleeding-related hospitalization was similarly reduced in the dual therapy group (5.1% vs 12.5%, p=0.04).

Table 3. Safety Outcomes Comparison

Outcome	Dual Therapy (n=118)	Triple Therapy (n=120)	p-value
Major bleeding, n (%)	9 (7.6)	21 (17.5)	0.03
Clinically relevant non-major bleeding, n (%)	17 (14.4)	30 (25.0)	0.04
Any bleeding event, n (%)	26 (22.0)	51 (42.5)	0.001
Bleeding-related hospitalization, n (%)	6 (5.1)	15 (12.5)	0.04

Multivariable analysis identified triple therapy as an independent predictor of major bleeding (adjusted OR 2.41, p=0.01). A HAS-BLED score ≥3 was also significantly associated with increased bleeding risk (adjusted OR 2.76, p=0.008). Chronic kidney disease independently predicted major bleeding (adjusted OR 1.92, p=0.04).

Table 4. Multivariable Predictors of Major Bleeding

Variable	Adjusted OR	95% CI	p-value
Triple therapy	2.41	1.18–4.92	0.01
HAS-BLED score ≥3	2.76	1.31–5.84	0.008
Age >75 years	1.69	0.84–3.38	0.14
Chronic kidney disease	1.92	1.01–3.64	0.04
Prior stroke	1.38	0.67–2.83	0.37

Subgroup analysis showed lower major bleeding rates with dual therapy in elderly patients aged ≥75 years (12.5% vs 29.4%, p=0.04) and in patients with HAS-BLED ≥3 (17.9% vs 40.0%, p=0.048).

Table 5. Subgroup Analysis of Clinical Outcomes by Treatment Strategy

Subgroup	Outcome	Dual Therapy n/N (%)	Triple Therapy n/N (%)	p-value
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Age ≥ 75 years	Major bleeding	4/32 (12.5)	10/34 (29.4)	0.04
Age < 75 years	Major bleeding	5/86 (5.8)	11/86 (12.8)	0.11
Diabetes mellitus	Thromboembolic events	5/48 (10.4)	5/51 (9.8)	0.92
Chronic kidney disease	Major bleeding	3/21 (14.3)	7/24 (29.2)	0.23
ACS patients	Major adverse cardiovascular events	8/52 (15.4)	10/55 (18.2)	0.70
PCI patients	Stent thrombosis	2/91 (2.2)	3/94 (3.2)	0.68
HAS-BLED ≥ 3	Major bleeding	5/28 (17.9)	12/30 (40.0)	0.048
CHA ₂ DS ₂ -VASc ≥ 4	Thromboembolic events	7/46 (15.2)	6/49 (12.2)	0.67

DISCUSSION

The current research compared the efficacy and safety of dual and triple antithrombotic therapy in patients with atrial fibrillation and coronary artery disease and proved that dual therapy had similar protection of thromboembolic and ischemic events with a significant decrease in bleeding complications. These results add to mounting evidence indicating that the attainment of safety by decreasing the intensity of antithrombotic use may not significantly decrease effectiveness in this high-risk group. Among the key results of this work, the similarity of thromboembolic events, myocardial infarction, stent thrombosis, and major adverse cardiovascular events was found in both dual and triple therapy groups, and it was not statistically significant. These findings indicate that exclusion of either antiplatelet agent in the dual therapy regimen had no statistically significant impact on exposing the patients to ischemic risk. This coincides with prior studies that have shown no greater harm of dual antithrombotic therapy compared to thromboembolic and coronary ischemic event prevention, although it makes treatment easier and less exposes the patient to the risk of bleeding [16].

One of the strengths of the findings is the safety outcomes. Significant reductions in major bleeding were observed in the dual therapy group than in triple therapy and non major bleeding of clinical relevance also decreased significantly. These results are consistent with the existing knowledge that triple therapy though used in the past to achieve maximum antithrombotic protection, has a high bleeding burden. The noted correlation between triple treatment and augmented hemorrhage in the multivariate examination additionally supports the unfavorable safety outcome of more vigorous antithrombotic control [17]. The decrease in the bleeding complications associated with dual therapy has clinical significance since bleeding complications in patients with AF and CAD are not harmless. Significant hemorrhage could lead to hospitalization, transfusion, antithrombotic therapy break, and a high risk of death. Moreover, the treatment discontinuation due to bleeding can have a contrary effect on thrombotic risk. Therefore, measures to minimize the blood loss without decreasing the effectiveness provide a valuable treatment benefit [18].

A significant result of this research was that dual therapy had a good profile even in subgroup analyses. Bleeding rates were lower with dual therapy in patients who had higher HAS-BLED scores, but thromboembolic outcomes were similar [19]. This observation helps to support the notion of dual therapy being possibly more useful with patients with a high hemorrhagic risk, which is a group of patients in which the treatment decisions can be the most difficult to make. The results of this study are in line with the previous randomized trials on the use of dual antithrombotic regimens, especially DOAC-based approaches, in which reduced bleeding has been established in comparison with triple therapy without compromising the efficacy. The same observations have informed current guideline recommendations to use shorter periods of triple therapy and to switch to dual therapy earlier in most patients with PCI. The current research provides additional evidence to these changing paradigms of treatment in a cohort study in the real world [20].

LIMITATIONS

There are several limitations to this study which must be kept in mind when interpreting the results. First, the retrospective design is prone to selection bias, missing data, and residual confounding because the allocation of treatment was not random and might have been affected by the preference of the physician, the risk of bleeding, or comorbidities. Baseline features were similar, but there could have been confounding unmeasured factors. Second, it was a single-center study, which might not be generalizable to other populations and healthcare environments. Third, the sample size of 238 patients could have been insufficient to pick up small differences in less common outcomes like stent thrombosis or mortality. Fluctuation in antithrombotic regimens, such as anticoagulant type variability, duration of therapy, and antiplatelet choice was also potentially influential but not individually examined. Moreover, treatment adherence and therapy modification during follow-up was not well evaluated.

CONCLUSION

It is concluded that dual antithrombotic therapy demonstrated comparable efficacy to triple antithrombotic therapy in preventing thromboembolic and ischemic events in patients with atrial fibrillation and coronary artery disease, while significantly reducing major and clinically relevant bleeding complications. These findings suggest that dual therapy provides a more favorable balance between safety and efficacy and may represent a preferred treatment strategy in appropriately selected patients, particularly those at increased bleeding risk.

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