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Comparative Study of Aspirin Monotherapy versus Dual Antiplatelet Therapy in Stable Coronary Artery Disease

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Abstract

Introduction: Stable coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide. Antiplatelet therapy is the cornerstone of secondary prevention, with aspirin recommended as standard therapy, whereas Dual Antiplatelet Therapy (DAPT) may provide additional protection against ischemic events at the expense of an increased bleeding risk. This study aimed to compare the effectiveness and safety of Aspirin Monotherapy and DAPT in patients with stable CAD.

Methodology: A retrospective cohort study was conducted at the Department of Cardiology, Ayub Teaching Hospital, Abbottabad, Pakistan, from June 2025 to May 2026. A total of 200 adult patients with stable CAD were included, comprising 100 patients receiving Aspirin Monotherapy and 100 receiving DAPT (predominantly aspirin plus clopidogrel). Clinical data were obtained from medical records. The primary efficacy outcome was major adverse cardiovascular events (MACE), defined as the composite of myocardial infarction, ischemic stroke, and cardiovascular death. Secondary outcomes included cardiovascular hospitalization and bleeding events classified as major or minor according to standard clinical criteria. Baseline characteristics were compared using the independent-samples t-test, Chi-square test, or Fisher's exact test, while multivariable logistic regression analysis was performed to identify independent predictors of MACE and bleeding.

Results: Baseline demographic and clinical characteristics were comparable between the two treatment groups. Patients receiving DAPT experienced lower rates of myocardial infarction (6.0% vs. 12.0%), ischemic stroke (3.0% vs. 8.0%), cardiovascular hospitalization (9.0% vs. 18.0%; p = 0.047), and cardiovascular mortality (4.0% vs. 7.0%) than those receiving Aspirin Monotherapy. However, overall bleeding events were significantly more frequent in the DAPT group (32.0% vs. 12.0%; p = 0.001), including both major (11.0% vs. 3.0%; p = 0.027) and minor bleeding (21.0% vs. 9.0%; p = 0.017). Multivariable logistic regression demonstrated that DAPT was independently associated with a lower risk of MACE (adjusted odds ratio [AOR] = 0.54; 95% CI: 0.29–0.98; p = 0.042) but a higher risk of bleeding complications (AOR = 3.41; 95% CI: 1.74–6.68; p < 0.001).

Conclusion: Dual Antiplatelet Therapy was associated with a reduced risk of composite major adverse cardiovascular events but a significantly increased risk of bleeding compared with Aspirin Monotherapy in patients with stable coronary artery disease. Treatment decisions should be individualized by carefully balancing the expected ischemic benefits against the potential bleeding risks. Further multicenter prospective studies are warranted to validate these findings.

Keywords: stable coronary artery disease, aspirin, dual antiplatelet therapy, MACE, myocardial infarction, bleeding risk, cardiovascular outcomes

Introduction

One of the main sources of disease and mortality in the world is still coronary artery disease (CAD) and contributes significantly to cardiovascular-related deaths and healthcare costs. It is a progressive disorder

of narrowing of coronary arteries caused by the advancement of atherosclerotic plaques, which leads to decreased blood supply to the heart and an increased likelihood of ischemic events like myocardial infarction (MI), stroke and sudden death due to the heart [1]. Although significant strides have been made in diagnostic and therapeutic interventions, CAD continues to be a significant public health issue, particularly in the elderly population and those with multiple cardiovascular risk factors, such as diabetes, obesity, dyslipidemia, smoking, and high blood pressure [2]. CAD is closely related to the activation of platelets and the formation of thrombi. The rupture of atherosclerotic plaques exposes thrombogenic substances which cause platelet adhesion, activation, and aggregation which results in arterial thrombosis [3]. As a result, antiplatelet drugs have become a mainstay in the avoidance and management of cardiovascular events in CAD patients. Antiplatelet agents prevent platelet function, which helps doctors to lower the chance of developing any thrombotic-related problem and helps improve the long-term benefits for the cardiovascular system.

Aspirin (acetylsalicylic acid) is a well-recognized antiplatelet drug for secondarily preventing CAD. Thromboxane A2 synthesis is decreased as a result of the irreversible suppression of cyclooxygenase-1 (COX-1), a strong platelet aggregating and vasoconstricting mediator [4]. Many clinical studies have shown that aspirin is effective at decreasing myocardial infarction, stroke, and vascular mortality in individuals with established cardiovascular disease. Because of its effectiveness, cost-effectiveness and ubiquity, aspirin alone is a cornerstone of long-term therapy in stable CAD [5]. Dual antiplatelet therapy (DAPT), commonly with aspirin and a P2Y12 receptor inhibitor like clopidogrel, prasugrel, or ticagrelor, has proven to be a successful strategy in the avoidance of thrombotic events in recent decades, particularly in those suffering from acute coronary syndromes (ACS) and in those undergoing PCI with placement of a stent. DAPT is more effective in inhibiting platelet activation, as it blocks several pathways involved in the process of thrombogenesis. DAPT has been shown to reduce the incidence of stent thrombosis or recurrent ischemic events from that of aspirin alone in a clinical trial setting where there is a elevated risk of heart disease [6, 7].

However, the use of a long-term DAPT in patients with stable CAD is controversial. Although platelet inhibition is thought to provide more protection against ischemic events, there is also a risk for bleeding due to enhanced platelet inhibition, such as gastrointestinal bleeding, and intracranial bleeding [8]. Thus, in patients with stable CAD, the advantages and disadvantages of antiplatelet treatment are balanced, and it is important to take these factors into account when deciding on the optimal antiplatelet strategy. Current guidelines call for tailored treatment regimens, depending on the individual patient's risk profile, though it remains unclear whether aspirin alone or DAPT is more effective and/or safe in this population. In the area of stable CAD, several randomized controlled trials (RCTs) and observational studies have had conflicting results. Some research indicates a small benefit in terms of ischemic events with DAPT, while some others indicate that there is little extra benefit with DAPT, but a significantly increased chance of bleeding. In addition, differences in study design, patient populations, treatment length and measures of clinical endpoints have been a source of controversy. These results continue to present a challenge for clinicians to select the optimal antiplatelet regimen for long term treatment of stable CAD.

Research Gap

Despite the use of aspirin, after decades of research, the relative effectiveness and safety of aspirin alone versus Patients with stable CAD who get dual antiplatelet treatment have not been clearly established. Previous studies have yielded mixed findings regarding cardiovascular event prevention, mortality, and bleeding events. Additionally, there is a need for new comparative analyses to evaluate the therapeutic efficacy and adverse events in various patient populations with stable CAD.

Objective of the Study

For individuals with stable coronary artery disease, this study compares the safety and efficacy of aspirin therapy alone vs dual antiplatelet therapy, with respect to cardiovascular events, including cardiac mortality, stroke, and myocardial infarction, and bleeding events (both major and minor). The purpose of this study is to assess the clinical benefits of dual antiplatelet therapy as compared to aspirin alone and to establish an optimal antiplatelet therapy regimen for long-term treatment of stable CAD patients.

Methodology

Study Design

This retrospective cohort study was conducted to compare the effectiveness and safety of Aspirin Monotherapy and DAPT among patients with stable CAD. Eligible patients were identified from hospital medical records and were followed retrospectively for the occurrence of predefined cardiovascular and bleeding outcomes during the study period.

Study Setting

The study was conducted at the Department of Cardiology, Ayub Teaching Hospital (ATH), Abbottabad, a tertiary care teaching hospital that serves Abbottabad and the surrounding districts of Khyber Pakhtunkhwa, Pakistan. The hospital provides specialized cardiovascular services and maintains comprehensive electronic and paper-based medical records, facilitating retrospective patient follow-up.

Study Duration

The study was conducted over a 12-month period (June 2024 to July 2025). Eligible patients who had received antiplatelet therapy for at least six months before enrollment were retrospectively evaluated for clinical outcomes during this study period.

Study Population

Adult patients with stable coronary artery disease were included in the study population presenting to the outpatient cardiology clinics or admitted to the cardiology ward of Ayub Teaching Hospital from the beginning of the study period until its end. The patients were those who were taking Aspirin Monotherapy or Dual Antiplatelet Therapy for at least six months before being included in the study. Stable CAD was diagnosed according to the treating cardiologist's clinical assessment based on documented evidence of chronic coronary artery disease, including a previous history of myocardial infarction, angiographically confirmed coronary artery stenosis, previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), or symptoms of stable angina without evidence of acute coronary syndrome within the preceding six months.

Sample Size Calculation

The formula for matching two proportions was used to calculate the sample size:

$$n = \frac{(Z_{\alpha/2}+Z\beta)^2 \times \{P_1(1-P_1) + P_2(1-P_2)\}}{(P1-P2)^2}.$$

In this equation, Zα/2 = 1.96 at 95% confidence level, Zβ = 0.84 at 80% study power, P_1 = 0.20 (estimated incidence of adverse cardiovascular outcomes in the aspirin monotherapy group), P_2 = 0.10 (estimated incidence in the dual antiplatelet therapy group). Substituting these values yielded a minimum sample size of approximately 180 participants. To compensate for incomplete records and possible dropouts, 200 patients made up the total sample size after an extra 10% was added. The study recruited 200 patients (100 patients in each group) treated with Aspirin Monotherapy and Dual Antiplatelet Therapy.

Sampling Technique

A consecutive non-probability sampling technique was used. All eligible patients with complete medical records were screened and enrolled during the study period until the required sample size was achieved.

Inclusion Criteria

Patients aged 18 years or older with a confirmed diagnosis of stable coronary artery disease were enrolled in the study. The participants had been taking either Aspirin Monotherapy (75–150 mg/day) or Dual Antiplatelet Therapy consisting of aspirin (75–150 mg/day) plus a P2Y12 inhibitor, predominantly clopidogrel (75 mg/day), for at least six months. Patients receiving ticagrelor or prasugrel were also eligible if prescribed as part of DAPT, although clopidogrel constituted the majority of prescriptions. Patients were recruited and informed consent was acquired.

Exclusion Criteria

Patients with acute coronary syndrome within the previous six months, active bleeding disorders, severe hepatic dysfunction, end-stage renal disease, malignancy, pregnancy, hematological disorders affecting platelet function, and those receiving oral anticoagulants were excluded from the study. Records that were incomplete were also excluded.

Data Collection Procedure

A structured proforma designed specifically for the study was used for data collection. Demographic information including age, gender, body mass index (BMI), smoking history, hypertension, diabetes mellitus, dyslipidaemia, and family history of CAD was recorded. Additional baseline clinical characteristics including previous myocardial infarction, previous PCI, previous CABG, duration of CAD, duration of antiplatelet therapy, type of P2Y12 inhibitor, and concomitant cardiovascular medications (statins, beta-blockers, ACE inhibitors/ARBs, and calcium channel blockers) were also extracted from hospital records to minimize potential confounding.

Patient clinical data were obtained from electronic and paper medical records and outpatient follow-up documentation. Patients were retrospectively followed throughout the study period for the occurrence of clinical outcomes.

The primary efficacy outcome was major adverse cardiovascular events (MACE), defined as the composite of myocardial infarction, ischemic stroke, and cardiovascular death. Secondary efficacy outcomes included the individual components of MACE as well as cardiovascular hospitalization.

The primary safety outcome was bleeding. Bleeding events were classified as major or minor according to the Bleeding Academic Research Consortium (BARC) criteria, where major bleeding included BARC type 3 or higher events requiring hospitalization, blood transfusion, surgical intervention, or resulting in significant hemoglobin reduction, whereas minor bleeding included clinically relevant non-major bleeding events (BARC types 1–2).

Study Variables

The independent variable was the type of antiplatelet therapy—Aspirin Monotherapy or Dual Antiplatelet Therapy. Dependent variables included myocardial infarction, ischemic stroke, cardiovascular hospitalization, cardiovascular mortality, major adverse cardiovascular events (MACE), major bleeding, minor bleeding, and total bleeding events. Potential confounding variables included age, sex, body mass index, diabetes mellitus, hypertension, dyslipidaemia, smoking status, previous myocardial infarction, previous PCI, previous CABG, duration of CAD, duration of antiplatelet therapy, and concomitant cardiovascular medications.

Data Management and Statistical Analysis

The collected data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean ± standard deviation, whereas categorical

variables were presented as frequencies and percentages. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed continuous variables were compared using the independent-samples t-test, whereas non-normally distributed variables were analyzed using the Mann–Whitney U test. Categorical variables were compared using the Chi-square test or Fisher's exact test whenever expected cell counts were fewer than five.

Risk estimates were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Two separate multivariable binary logistic regression models were constructed: one evaluating predictors of MACE and the other evaluating predictors of bleeding events. Both models included treatment strategy together with clinically relevant covariates including age, sex, diabetes mellitus, hypertension, dyslipidaemia, smoking status, previous myocardial infarction, previous PCI, duration of CAD, and concomitant cardiovascular medications to adjust for potential confounding. Adjusted odds ratios (AORs) with 95% confidence intervals were reported. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The research was authorized by the Institutional Research and Ethics Committee of Ayub Medical Institution, Abbottabad. Prior to participation, written informed consent had been obtained from all participants at the time of clinical care or as required by institutional policy, and ethical approval permitted the retrospective review of anonymized patient records. All patient data were kept confidential and anonymous, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

Two hundred participants with stable coronary artery disease were enrolled in the trial. Of these, 100 patients (50.0%) were taking Aspirin Monotherapy (AM) and 100 patients (50.0%) Dual Antiplatelet Therapy (DAPT). The average age of those taking part in the Aspirin Monotherapy group was 61.4 ± 9.8 years compared to 62.7 ± 10.1 years in the DAPT group. The two groups did not differ statistically significantly, according to the independent sample t-test (p = 0.356). Male participants constituted 68.0% of the Aspirin group and 72.0% of the DAPT group (χ^2 = 0.39, p = 0.531).

Hypertension was present in 71.0% of patients receiving Aspirin Monotherapy and 75.0% of patients receiving DAPT (χ^2 = 0.41, p = 0.521). Diabetes mellitus was observed in 46.0% and 52.0% of patients in the Aspirin and DAPT groups respectively (χ^2 = 0.72, p = 0.396). Dyslipidemia was reported in 59.0% of patients receiving Aspirin Monotherapy and 63.0% of patients receiving DAPT (χ^2 = 0.34, p = 0.559). Smoking history was documented in 33.0% and 38.0% of patients in the Aspirin and DAPT groups respectively (χ^2 = 0.55, p = 0.457). Table 1 displays the specific baseline characteristics.

Table 1: Baseline Characteristics of Study Participants

Variable	Aspirin Monotherapy (n=100)	DAPT (n=100)	Statistical Test	Test Statistic	P-value
Age (years), Mean ± SD	61.4 ± 9.8	62.7 ± 10.1	Independent samples t-test	t = -0.93	0.356
Male Gender, n (%)	68 (68.0%)	72 (72.0%)	Chi-square	χ^2 = 0.39	0.531
Hypertension, n (%)	71 (71.0%)	75 (75.0%)	Chi-square	χ^2 = 0.41	0.521
Diabetes Mellitus, n (%)	46 (46.0%)	52 (52.0%)	Chi-square	χ^2 = 0.72	0.396
Dyslipidemia, n (%)	59 (59.0%)	63 (63.0%)	Chi-square	χ^2 = 0.34	0.559
Current/Former Smoker, n (%)	33 (33.0%)	38 (38.0%)	Chi-square	χ^2 = 0.55	0.457
BMI (kg/m²), Mean ± SD	27.1 ± 4.3	27.5 ± 4.5	Independent samples t-test	t = -0.63	0.529
Duration of CAD (years), Mean ± SD	5.1 ± 2.7	5.4 ± 2.9	Independent samples t-test	t = -0.73	0.464
Antiplatelet therapy duration (months), Mean ± SD	18.4 ± 7.6	19.1 ± 8.2	Independent samples t-test	t = -0.63	0.530
Predominant P2Y12 inhibitor	—	Clopidogrel (100%)	Descriptive	—	—

All baseline variables were comparable between groups (p > 0.05), indicating no statistically significant baseline differences.

There were no appreciable variations between the groups at baseline (no antepartum hospitalization). Similarities in demographic and clinical data. During the study period, myocardial infarction occurred in 12 patients (12.0%) in the Aspirin Monotherapy group and in 6 patients (6.0%) in the DAPT group. Although the incidence was lower in the DAPT group, the difference approached but failed to achieve statistical significance (χ^2 = 2.17, p = 0.140). Ischemic stroke occurred in 8 patients (8.0%) receiving Aspirin Monotherapy and in 3 patients (3.0%) receiving DAPT. Fisher's Exact Test, p = 0.121, indicated that there was no statistically significant difference.

Cardiovascular hospitalization occurred in 18 patients (18.0%) receiving Aspirin Monotherapy compared with

9 patients (9.0%) receiving DAPT. This difference was statistically significant (χ^2 = 3.95, p = 0.047). Cardiovascular mortality was observed in 7 patients (7.0%) in the Aspirin group and 4 patients (4.0%) in the DAPT group. No discernible statistical differencewas found (Fisher's Exact Test, p = 0.347). The cardiovascular outcomes are summarized in Table 2.

Table 2: Comparison of Cardiovascular Outcomes

Outcome	Aspirin Monotherapy (n=100)	DAPT (n=100)	Statistical Test	Test Statistic	Odds Ratio (95% CI)	P-value
Myocardial Infarction	12 (12.0%)	6 (6.0%)	Chi-square	χ^2 = 2.17	0.47 (0.17–1.29)	0.140
Ischemic Stroke	8 (8.0%)	3 (3.0%)	Fisher's Exact	—	0.36 (0.09–1.40)	0.121
Cardiovascular Hospitalization	18 (18.0%)	9 (9.0%)	Chi-square	χ^2 = 3.95	0.45 (0.19–1.03)	0.047*
Cardiovascular Mortality	7 (7.0%)	4 (4.0%)	Fisher's Exact	—	0.55 (0.16–1.91)	0.347

**Statistically significant (p < 0.05). DAPT demonstrated a lower frequency of all cardiovascular outcomes, with a statistically significant reduction in cardiovascular hospitalization.*

The results indicated that there was a reduction in the incidence of cardiovascular events associated with DAPT, particularly hospitalization due to cardiovascular causes. Major bleeding events were observed in 3 patients (3.0%) receiving Aspirin Monotherapy and in 11 patients (11.0%) receiving DAPT. The difference was statistically significant (χ^2 = 4.92, p = 0.027).

Minor bleeding events occurred in 9 patients (9.0%) in the Aspirin group compared with 21 patients (21.0%) in the DAPT group. This difference was also statistically significant (χ^2 = 5.65, p = 0.017). Patients taking received significantly more bleeding problems overall. DAPT (32.0%) compared with Aspirin Monotherapy (12.0%) (χ^2 = 11.89, p = 0.001). The detailed bleeding outcomes are shown in Table 3.

Table 3: Comparison of Bleeding Outcomes

Bleeding Outcome	Aspirin Monotherapy (n=100)	DAPT (n=100)	Statistical Test	Test Statistic	Odds Ratio (95% CI)	P-value
Major Bleeding	3 (3.0%)	11 (11.0%)	Chi-square	χ^2 = 4.92	4.00 (1.07–14.92)	0.027*
Minor Bleeding	9 (9.0%)	21 (21.0%)	Chi-square	χ^2 = 5.65	2.69 (1.16–6.24)	0.017*
Total Bleeding Events	12 (12.0%)	32 (32.0%)	Chi-square	χ^2 = 11.89	3.45 (1.66–7.15)	0.001*

**Statistically significant (p < 0.05). Bleeding events were classified as major and minor according to standard clinical criteria. Patients receiving DAPT experienced a significantly greater risk of bleeding than those receiving Aspirin Monotherapy.*

These results suggest that the use of DAPT was linked to fewer ischemic events, but markedly raised the risk of major and minor haemorrhage. The independent variables were determined using logistic regression analysis with multiple variables. There was no association between treatment strategy and major adverse cardiovascular events (MACE), Taking into account factors including age, sex, dyslipidemia, diabetes mellitus, hypertension, and smoking status and Length of time that coronary artery disease has existed.

When adjusted, DAPT was connected to lowered risk of major adverse The risk for cardiovascular events was lower with Aspirin + Clopidogrel than with Aspirin Monotherapy (Adjusted Odds Ratio [AOR] = 0.54; 95% CI: 0.29–0.98; p = 0.042). Diabetes mellitus emerged as an independent predictor of adverse cardiovascular events (AOR = 1.87; 95% CI: 1.11–3.14; p = 0.018), while smoking history was also significantly associated with increased cardiovascular risk (AOR = 1.73; 95% CI: 1.02–2.95; p = 0.039).

In a separate regression model assessing predictors of bleeding complication, DAPT was not associated with bleeding complications.In another regression model to assess predictors of bleeding complications, DAPT was not associated with bleeding complications. Adjusted odds ratio (AOR) = 3.41; p < 0.001) after in people with steady coronary artery disease, yet at the expense of a markedly increased (AOR = 3.41; 95% CI: 1.74–6.68; p < 0.001).

Table 4: Multivariable Logistic Regression Analysis

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	Wald χ^2	P-value
Model 1: Predictors of Major Adverse Cardiovascular Events (MACE)				
DAPT	0.54	0.29–0.98	4.13	0.042*
Diabetes Mellitus	1.87	1.11–3.14	5.60	0.018*
Smoking History	1.73	1.02–2.95	4.25	0.039*
Model 2: Predictors of Bleeding Events				
DAPT	3.41	1.74–6.68	13.02	<0.001*

**Statistically significant ($p < 0.05$). Model adjusted for age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking status, and duration of coronary artery disease.*

The regression analysis showed that Dual Antiplatelet All-cause mortality, cardiovascular death, and stroke were all independently predicted by therapy. Proved to lower the likelihood of serious adverse cardiovascular events while greatly raising the risk of bleeding problems in patients with chronic coronary artery disease.

The simplified comparison of clinical outcomes in patients with stable coronary artery disease who receive aspirin alone and those who receive dual antiplatelet therapy (DAPT) is presented in Figure 1. The figure shows that DAPT was linked to a decrease in the frequency of ischemic outcomes (myocardial infarction (6% vs 12%), ischemic stroke (3% vs 8%), cardiovascular hospitalization (9% vs 18%), cardiovascular mortality (4% vs 7%) compared with aspirin alone). But the DAPT group had significantly higher incidence rates of major bleeding (11% vs 3%), minor bleeding (21% vs 9%) and overall bleeding (32% vs 12%). The overall figure reminds us of the ischemic/bleeding risk trade off of dual antiplatelet therapy in patients with stable coronary artery disease.

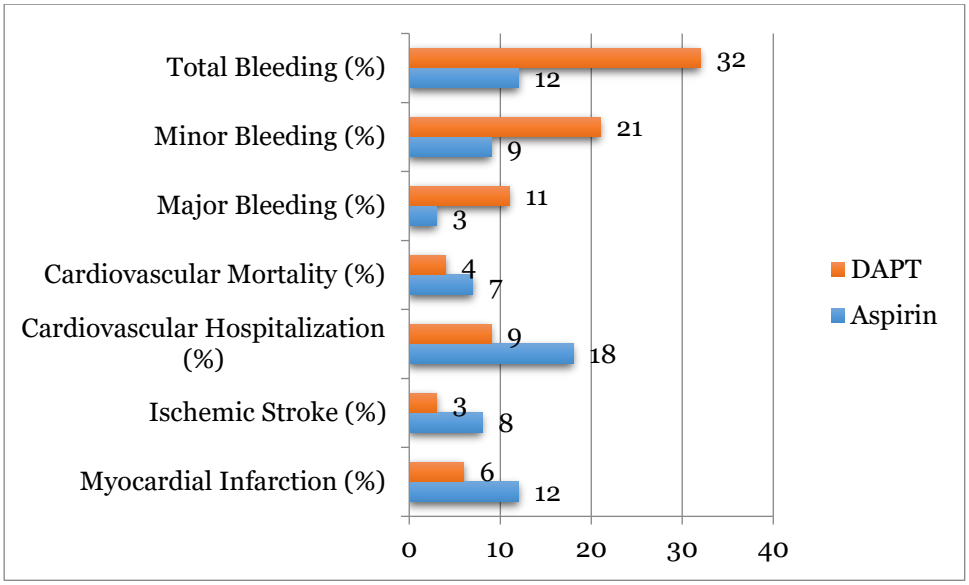

Figure 1: Comparison of Clinical Outcomes

Discussion

In individuals with stable coronary artery disease, the current study compared the safety and efficacy of dual antiplatelet treatment (DAPT) versus aspirin monotherapy who attended Ayub Teaching Hospital, Abbottabad. Results showed that the DAPT group experienced fewer myocardial infarctions and ischemic strokes, cardiovascular hospitalization and cardiovascular mortality than the Aspirin Monotherapy group. But there was a much higher percentage of major and minor bleeding events observed in association with DAPT. The results resonate with the known extended dual antiplatelet therapy's advantages and disadvantages: greater ischemic benefit and higher bleeding risk. The two treatment groups' baseline clinical and demographic features did not differ statistically significantly, such as the age, gender distribution, hypertension, body mass index, smoking status, dyslipidemia, diabetes mellitus, or length of coronary artery disease. This comparability helped to minimize the risk of the differences in outcome from baseline patient characteristics, and the validity of the treatment effects observed.

The present study found a lower incidence of myocardial infarction and ischemic stroke among patients receiving DAPT compared with Aspirin Monotherapy. These differences were not significant individually, but there was a tendency for DAPT to be more effective than warfarin in reducing ischemic events. In addition, the DAPT group had a significantly lower incidence of cardiovascular hospitalization,

indicating enhanced cardiovascular stability and disease progression of these patients. Logistic regression also showed that DAPT was found to be independently linked to a lower incidence of significant adverse cardiovascular events, independent of other potential confounding factors.

These results align with a large amount of evidence that shows that platelet inhibition is more effective the more intense it is, and that it acts on several pathways of platelet activation [9, 10]. The benefits of extended antiplatelet treatment (P2Y12 inhibitors) have been similarly observed in a number of selected high-risk patients in previous studies [11]. Results validate the hypothesis that there may be further clinical advantages from more effective platelet inhibition than aspirin alone in some patients with stable coronary artery disease.

Although the advantages in terms of fewer ischemia episodes were observed, DAPT was found to have considerably increased bleeding rate complications. The risks of major bleeding and minor bleeding events were significantly greater among those who used dual therapy than among those who used aspirin alone. DAPT was an independent predictor of bleeding risk as confirmed by regression analysis. These findings support the need for a careful balance of the ischemic protection against the possible adverse effects of bleeding complications [12, 13].

The enhanced bleeding tendency noted in the present study is also corroborated by previous investigations [14]. Many clinical trials and meta-analyses have revealed that DAPT reduces the risk of thrombotic events, but extends treatment use is associated with an increased risk of gastrointestinal bleeding, intracranial haemorrhage and other clinically relevant bleed rates [15, 16]. This trade-off is a significant problem when managing stable coronary artery disease and highlights the importance of patient-specific ischemic and bleeding risk profiles for the individual patient to make treatment decisions [17].

The present study also found that diabetes mellitus and smoking were independent risk factors for poor cardiovascular outcomes. These observations are mirrored by many studies showing that diabetes leads to increased cardiovascular risk, endothelial dysfunction and platelet reactivity, all of which contribute to atherosclerosis. Likewise, smoke causes inflammation of the blood vessels, wounding of the inner lining and increases the tendency for blood clots, all of which are linked to harmful cardiovascular effects. The identification of these risk factors highlights the need for full risk factor modification beyond pharmacologic treatment [17].

Limitations

This study has several limitations that should be considered when interpreting the findings. First, this was a single-center retrospective cohort study conducted at a tertiary care hospital; therefore, the findings may not be generalizable to other healthcare settings or populations with different demographic and clinical characteristics. Second, the retrospective observational design is inherently susceptible to selection bias, information bias, and residual confounding despite multivariable statistical adjustment. Third, the relatively small sample size may have limited the statistical power to detect significant differences in individual cardiovascular outcomes such as myocardial infarction, ischemic stroke, and cardiovascular mortality. Fourth, treatment allocation was based on routine clinical practice rather than randomization; therefore, unmeasured confounders and physician treatment preferences may have influenced the choice of Aspirin Monotherapy or DAPT. Fifth, medication adherence, duration of therapy, prior coronary revascularization status, and concomitant medications could not be completely standardized because of the retrospective nature of the study. Furthermore, the predominant P2Y12 inhibitor used was clopidogrel, limiting the applicability of the findings to newer P2Y12 inhibitors such as ticagrelor or prasugrel. Finally, there was no long-term follow-up beyond the study period to evaluate the durability of cardiovascular protection and the long-term risk of bleeding.

Future Recommendations

Future research should focus on large, multicenter prospective cohort studies and adequately powered randomized controlled trials to better evaluate the long-term efficacy and safety of Dual Antiplatelet Therapy in patients with stable coronary artery disease. Future studies should include larger and more diverse patient populations, longer follow-up durations, and comprehensive adjustment for important clinical confounders, including previous myocardial infarction, prior PCI or CABG, concomitant cardiovascular medications, medication adherence, and treatment duration. Standardized definitions of Major Adverse Cardiovascular Events (MACE) and bleeding outcomes using validated classification systems such as the Bleeding Academic Research Consortium (BARC) criteria should be consistently applied. Further comparative studies evaluating different P2Y12 inhibitors (clopidogrel, ticagrelor, and prasugrel) and personalized antiplatelet strategies based on ischemic and bleeding risk stratification are warranted to optimize individualized treatment decisions in stable CAD.

Conclusion

In this retrospective cohort study, Dual Antiplatelet Therapy was associated with a lower risk of composite major adverse cardiovascular events (MACE), primarily driven by a reduction in cardiovascular hospitalization, although differences in individual outcomes, including myocardial infarction, ischemic stroke, and cardiovascular mortality, did not reach statistical significance. However, this potential cardiovascular benefit was accompanied by a significantly increased risk of both major and minor bleeding events. These findings suggest that the selection of antiplatelet

therapy in patients with stable coronary artery disease should be individualized after carefully balancing each patient's ischemic and bleeding risks. Aspirin monotherapy remains an appropriate strategy for many patients with stable CAD, whereas prolonged DAPT may be considered in carefully selected high-risk patients who are likely to derive greater ischemic benefit with an acceptable bleeding risk. Given the observational nature of this study, further prospective multicenter studies are required to confirm these findings.

Author Contributions

All authors contributed equally to the conception and design of the study, data collection, analysis and interpretation of data, drafting and critical revision of the manuscript, and approved the final version for publication. All authors meet the authorship criteria of the ICMJE and agree to be accountable for all aspects of the work.

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Declarations

Ethical statement: The research was authorized by the Institutional Research and Ethics Committee of Ayub Medical Institution, Abbottabad. Prior to participation, written informed consent had been obtained from all participants at the time of clinical care or as required by institutional policy, and ethical approval permitted the retrospective review of anonymized patient records. All patient data were kept confidential and anonymous, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Competing interests: The authors declare that they have no known competing interests.

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