

Article

Ticagrelor or Clopidogrel After PCI in Atrial Fibrillation? Insights from a Real-World Retrospective Analysis

Ferhat Siyamend Yurdam *  and Ahmet Anıl Başkurt 

Department of Cardiology, Bakırçay University Çiğli Training and Research Hospital, 35620 Izmir, Turkey; a.baskurt@windowslive.com

* Correspondence: fyurdam83@hotmail.com; Tel.: +90-5533186402

Abstract

Background: Optimal antithrombotic therapy in patients with AF undergoing PCI while receiving OAC remains a clinical challenge. Although clopidogrel is generally recommended as the preferred P2Y₁₂ inhibitor in this setting, evidence comparing clopidogrel with ticagrelor in real-world AF-PCI populations is limited. **Objective:** To evaluate ischemic and bleeding outcomes in AF patients treated with DOAC combined with clopidogrel, ticagrelor, or TAT following PCI for ACS. **Methods:** This study involved 248 consecutive patients with non-valvular AF who underwent PCI for ACS and were discharged on DOAC plus clopidogrel (Group 1), DOAC plus ticagrelor (Group 2), or aspirin + clopidogrel + DOAC (Group 3). Cox regression analysis was used to determine the difference in survival rates among the three groups regarding the composite ischemic endpoint (stroke, MI, and stent restenosis) and bleeding. **Results:** In the Cox regression analysis performed, no statistically significant effect of the variables representing the antiplatelet treatment groups on ischemic outcomes was observed during the 1-year follow-up (Wald = 3.681; df = 2; $p = 0.159$). **Conclusions:** In this retrospective real-world cohort of AF patients undergoing PCI for ACS, clopidogrel-based dual therapy appeared to provide clinical outcomes comparable to ticagrelor with respect to thromboembolic and bleeding events. No clear ischemic advantage of ticagrelor was observed, although a numerical increase in minor bleeding was noted.

Keywords: non-valvular AF; acute coronary syndrome; percutaneous coronary intervention; antiplatelet therapy; DOAC

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. The use of oral anticoagulant (OAC) therapy in AF carries a substantial risk of bleeding, and balancing this risk against the prevention of thromboembolic events remains a major challenge during long-term management [1]. The proportion of patients with AF who undergo percutaneous coronary intervention (PCI) is not negligible, ranging from 5% to 8% in large registries [2]. In these patients, optimal antithrombotic therapy requires careful consideration to prevent both ischemic and bleeding complications.

To reduce the risk of stent thrombosis, dual antiplatelet therapy is recommended in addition to OAC for a certain period. According to current European Society of Cardiology (ESC) guidelines, patients undergoing PCI for acute coronary syndrome (ACS) should receive antiplatelet therapy for 12 months, whereas those undergoing PCI for chronic coronary syndrome (CCS) should receive it for at least 6 months [3]. Therefore, a meticulous



Academic Editor: Ardan Muammer Saguner

Received: 2 July 2026

Revised: 29 July 2026

Accepted: 31 July 2026

Published: 3 August 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

assessment of each patient's ischemic and bleeding risk is essential to determine the most appropriate combination and duration of OAC and antiplatelet therapy [1,4].

Previous studies have generally favored clopidogrel as the preferred P2Y₁₂ inhibitor in patients receiving OAC due to its lower bleeding risk profile [1,4]. However, in individuals with high ischemic risk, more potent antiplatelet agents such as ticagrelor may be required to ensure adequate platelet inhibition, particularly during the early post-PCI period when the risk of stent thrombosis is highest.

The present study aims to determine which P2Y₁₂ inhibitor—ticagrelor or clopidogrel—is more effective and safer when combined with oral anticoagulation in patients with non-valvular AF undergoing PCI for ACS. Specifically, we sought to evaluate whether the choice of antiplatelet agent affects the long-term incidence of major adverse cardiovascular events (MACEs), including stroke, myocardial infarction, and death, as well as the risk of bleeding complications.

2. Material and Methods

This retrospective observational study included consecutive patients who were admitted to the cardiology department between January 2017 and October 2024 for acute coronary syndrome (ACS), underwent coronary angiography, and subsequently received percutaneous coronary intervention (PCI). All included patients had a prior diagnosis of non-valvular AF requiring oral anticoagulant (OAC) therapy.

To minimize the influence of acute procedural events and early treatment modifications, patients who died or experienced major procedural complications during the first 7 days after PCI were excluded. Antithrombotic treatment groups were defined according to the regimen prescribed at hospital discharge (or day 7 if modified during hospitalization), and follow-up for clinical outcomes started thereafter.

During the first 7 days after PCI, all patients received aspirin together with a P2Y₁₂ inhibitor (either clopidogrel or ticagrelor) and therapeutic-dose low-molecular-weight heparin. After this initial treatment phase, patients were classified according to their maintenance antithrombotic regimen: Group 1: Direct oral anticoagulant (DOAC) plus clopidogrel. Group 2: Direct oral anticoagulant (DOAC) plus ticagrelor. Group 3: Triple antithrombotic therapy consisting of aspirin, clopidogrel, and a DOAC for one month. After one month, aspirin was discontinued, and patients continued treatment with clopidogrel plus a DOAC.

Ethics committee approval for our study was received from our University Non-Interventional Ethics Committee with the date and number: 28 November 2024-1872.

2.1. Inclusion and Exclusion Criteria

Patients aged 18–80 years who underwent successful PCI for ACS and were on OAC therapy for non-valvular AF were eligible.

Exclusion criteria included:

- History of stroke or transient ischemic attack (TIA).
- Hemoglobin < 10 g/dL.
- Severe renal impairment (Glomerular filtration rate < 30 mL/min/1.73 m²).
- Severe hepatic dysfunction (defined as serum transaminases > 3× the upper reference limit or clinical evidence of hepatic failure).
- Prosthetic or bioprosthetic heart valves.
- Current use of vitamin K antagonists (VKA).
- CHA₂DS₂-VA score < 1 point.
- Death or major procedural complication during the first-week blank period.
- Patients with indications for DOACs for reasons other than AF.

2.2. Data Collection

Demographic characteristics, comorbidities, angiographic findings, and laboratory results were retrieved from the institutional electronic medical database. Post-discharge pharmacotherapy and adverse clinical outcomes were reviewed. Bleeding events were classified as major or minor according to Bleeding Academic Research Consortium (BARC) ≥ 2 criteria.

MACEs were defined based on ischemic endpoints as revascularization due to stent restenosis, MI following PCI, and stroke. Additionally, patients identified as having major or minor bleeding were defined and reported regarding the primary endpoint. If patients experienced both ischemic and bleeding outcomes during the 12-month follow-up after PCI, these events were recorded separately.

If a patient experienced more than one ischemic event, this was recorded as a single case. In the event of an adverse outcome, DOAC therapy was not changed; specifically, in cases of ischemic events, the antiplatelet agent was replaced with a more potent one, whereas in cases of bleeding, it was replaced with a less potent agent.

3. Statistical Analysis

All statistical analyses were conducted using SPSS for Windows, version 24.0 (IBM Corp., Armonk, NY, USA). The normality of the distribution of numerical variables was tested using the Kolmogorov–Smirnov (if $n \geq 50$) and Shapiro–Wilk (if $n < 50$) statistical tests. The Levene test was applied to assess the homogeneity of the data distribution. Since the distribution of numerical variables across the groups differed significantly, the analysis was continued using the Kruskal–Wallis test. Continuous variables are expressed as median and IQR (25–75). Categorical variables are presented as frequencies and percentages and were compared using the chi-square test (if $n \geq 5$) or Fisher’s exact test (if $n < 5$). Cox regression analysis was used to determine the difference in survival rates among the three groups regarding the composite ischemic endpoint (stroke, MI, and stent restenosis) and bleeding. A two-sided p -value < 0.05 was considered statistically significant.

4. Results

A total of 248 consecutive patients receiving oral anticoagulant therapy for non-valvular atrial fibrillation who underwent PCI for acute coronary syndrome were included in the study. The mean age and sex distribution were 62 (56–70) years (49% male) in Group 1 and 63.5 (57–69) years (65% male) in Group 2, 62 (59–65) years (60% male) in Group 3, with no significant difference between the groups ($p = 0.87$ vs. $p = 0.24$, respectively).

Among all patients, 54% had hypertension ($n = 136$), 43% had diabetes mellitus ($n = 106$), 8% had reduced EF heart failure (HFrEF) ($n = 20$), and 4% had vascular disease ($n = 10$), with no statistically significant intergroup differences.

During follow-up after ACS, 6 patients (4%) in Group 1, 4 patients (5%) in Group 2 and 2 patients in Group 3 (10%) required coronary revascularization due to restenosis ($p = 0.41$), the same number of patients in each group experienced stroke and MI ($p = 0.19$).

In terms of bleeding complications, major bleeding was observed in 4 patients in groups 1 and 2, while it occurred in 2 patients in group 3 ($p = 0.18$). Minor bleeding was observed in 14 patients (9.5%) in Group 1, 18 patients (23%) in Group 2, and 4 patients (20%) in Group 3, but no statistically significant difference was observed ($p = 0.17$).

Table 1 summarizes the patients’ demographic and clinical characteristics and comorbidities. While Table 2 presents angiographic data for both groups, Table 3 includes clinical outcomes, Table 4 the patients’ current medication use, and Table 5 detailed hematological and biochemical laboratory analyses.

Table 1. Basic clinical features, demographic data.

Variables	Group 1 (n = 148)	Group 2 (n = 80)	Group 3 (n = 20)	p Value
Age, Median and IQR (25–75), years	62 (56–70)	63.5 (57–69)	62 (59–65)	0.87
Male, n (%)	72 (49)	52 (65)	12 (60)	0.24
BMI, Median and IQR (25–75), kg/m ²	23 (20.8–26.1)	23 (21.5–26.3)	21 (20.2–22.8)	0.08
CHADSVA score, Median and IQR (25–75)	2 (2–3)	3 (2–3)	3 (2–3)	0.94
Hypertension, n (%)	82 (55)	42 (53)	12 (60)	0.90
Diabetes mellitus, n (%)	66 (45)	34 (43)	6 (30)	0.68
Smoking, n (%)	58 (39)	26 (33)	8 (40)	0.76
HFrEF, n (%)	8 (5.4)	10 (13)	2 (10)	0.40
Vascular disease, n (%)	2 (1.4)	6 (7.5)	2 (10)	0.17

Table 2. Coronary interventional procedural data.

Variables	Group 1 (n = 148)	Group 2 (n = 80)	Group 3 (n = 20)	p Value
MI type, n (%)				
NSTEMI	80 (54)	46 (58)	14 (70)	0.63
STEMI	68 (46)	34 (43)	6 (30)	
Infarct-related artery, n (%)				
Left main coronary artery	6 (4)	4 (5)	2 (10)	0.91
Left descending artery	60 (41)	36 (45)	8 (40)	
Circumflex artery	38 (26)	14 (18)	6 (30)	
Right coronary artery	44 (30)	26 (33)	4 (20)	
Stent (mean ± SD), Median and IQR (25–75), mm				
Diameter	3 (2.75–3)	3 (2.88–3)	3 (2.88–3)	0.30
Length	20 (16–24)	24 (20–28)	26 (19–32)	0.09
Balloon predilatation, n (%)	140 (95)	72 (90)	18 (90)	0.63
Balloon postdilatation, n (%)	132 (89)	70 (88)	14 (70)	0.24
Balloon diameter, mm	3 (2.75–3)	3 (2.75–3)	3 (2.62–3.25)	0.29
Balloon length, mm	15 (12–15)	15 (12–15)	15 (12–16.5)	0.92
Thrombus score	1 (0–3)	1 (0–3)	1 (0–2.5)	0.60
Thrombectomy during procedure, n (%)	18 (12)	8 (10)	2 (10)	0.93
Glycoprotein 2b/3a antagonist, n (%)	34 (23)	18 (23)	2 (10)	0.64

Table 3. Clinical outcomes.

Variables	Group 1 (n = 148)	Group 2 (n = 80)	Group 3 (n = 20)	p Value
Ischemic MACEs, n (%)	14 (9.4)	8 (10)	5 (30)	0.11
Revascularization due to stent restenosis	6 (4)	4 (5)	2 (10)	0.41
MI after PCI	4 (2.7)	2 (2.5)	2 (10)	0.19
Stroke after PCI	4 (2.7)	2 (2.5)	2 (10)	0.19
Outcome involving bleeding, n (%)				
Minor	14 (9.5)	18 (23)	4 (20)	0.17
Major	4 (2.7)	4 (5)	2 (10)	0.18

SD: standard deviation, n: number of patients, BMI: body mass index, HFrEF: reduced EF heart failure, MI: myocardial infarction, MACE: major adverse cardiovascular event, PCI: percutaneous coronary intervention, Group 1: DOAC + Clopidogrel (+), Group 2: DOAC + Ticagrelor (+), Group 3: (TAT) triple antiplatelet therapy (+).

Table 4. Cardiac medication of patients.

Drugs <i>n</i> (%)	Group 1 (<i>n</i> = 148)	Group 2 (<i>n</i> = 80)	Group 3 (<i>n</i> = 20)	<i>p</i> Value
Beta-blocker therapy	134 (91)	70 (88)	16 (80)	0.59
Statin	140 (94)	76 (95)	18 (90)	0.82
RAS blocker	82 (55)	46 (58)	16 (80)	0.33
<i>Anticoagulants</i>				
Apixaban	50 (34)	28 (35)	6 (30)	0.98
Rivaroxaban	66 (45)	34 (43)	8 (40)	
Edoxaban	32 (22)	18 (23)	6 (30)	

n: number of patients, RAS: renin-angiotensin-system, Group 1: DOAC + Clopidogrel, Group 2: DOAC + Ticagrelor, Group 3: (TAT) triple antiplatelet therapy.

Table 5. Blood analysis of hematological and biochemical parameters.

Variables (Median and IQR (25–75))	Group 1 (<i>n</i> = 148)	Group 2 (<i>n</i> = 80)	Group 3 (<i>n</i> = 20)	<i>p</i> Value
Glucose, mg/dL	96 (89–108)	96 (89–113)	106 (101–133)	0.11
Urea, mg/dL	10.5 (8.7–15.8)	11.1 (8.3–19.7)	17 (16–23)	0.16
AST, U/L	18 (16–22)	17 (13–21.5)	24 (21.5–25.5)	0.15
ALT, U/L	19 (13–25)	18.5 (13–23.5)	24 (21.5–25)	0.23
Creatinine, mg/dL	0.97 (0.81–1.16)	0.95 (0.77–1.24)	0.95 (0.88–1.1)	0.98
GFR (first time), mL/min	70.8 (60.9–89)	74.3 (57.2–91.4)	79.8 (64.7–87.5)	0.77
GFR (1st month), mL/min	74.6 (63.2–96.4)	80 (60.5–95.9)	65.6 (60.5–80.7)	0.63
GFR (6th month), mL/min	75.2 (62.4–94.3)	79.4 (63.3–92.7)	63 (57.7–72.6)	0.27
Hemoglobin (first time), gr/dL	13.2 (12.1–14.7)	12.5 (11.3–14.1)	12 (11.8–13.6)	0.32
Hemoglobin (1st month), gr/dL	12.7 (11.6–14.2)	12 (10.8–13.6)	11.6 (11.4–12.7)	0.29
Hemoglobin (6th month), gr/dL	12.7 (11.3–14)	12 (10.7–13.6)	11 (10.9–12.2)	0.19
Htc (first time), %	38 (35–43)	36.7 (33–42)	37.1 (35–40.1)	0.57
Htc (1st month), %	37.4 (34.2–41.8)	35.4 (31.9–40.1)	34.9 (33.7–37.4)	0.29
Htc (6th month), %	37.7 (33.7–41.7)	35.8 (31.9–40.5)	32.9 (32.6–36.4)	0.21
Platelet (first time), $\times 10^3$ /L	239 (207–289)	218 (204–264)	222 (204–260)	0.54
Platelet (1st month), $\times 10^3$ /L	229 (208–274)	228 (205–268)	212 (203–249)	0.79
Platelet (6th month), $\times 10^3$ /L	231 (209–279)	223 (208–272)	218 (190–230)	0.70

SD: standard deviation, GFR: glomerular filtration rate, Htc: hematocrit, Group 1: DOAC + Clopidogrel (+), Group 2: DOAC + Ticagrelor (+), Group 3: TAT (triple antiplatelet therapy).

In the Cox regression analysis (Figure 1) performed, no statistically significant effect of the variables representing antiplatelet treatment groups on the ischemic outcome was observed. (Wald = 3.681, *df* = 2, *p* = 0.159). Compared to Group 1, although the hazard ratio (HR) for patients in Group 2 showed a trend towards being lower, the difference did not reach statistical significance (HR = 0.38, 95% CI [0.14–1.06], *p* = 0.064). Similarly, it was found that Group 3 did not show a significant difference compared to Group 1 regarding ischemic outcomes (HR = 0.40, 95% CI [0.13–1.21], *p* = 0.105).

In the Cox regression analysis performed (Figure 2), no statistically significant effect of the variables representing the antiplatelet treatment groups on the major bleeding outcome was observed (Wald = 3.146; *df* = 2; *p* = 0.169). Compared to Group 1, no significant increase in risk was observed in patients in Group 2 (HR = 2.23, 95% CI [0.56–8.92], *p* = 0.258). Although the risk for patients in Group 3 appeared to be approximately 4.4 times higher than that of Group 1, this difference did not reach statistical significance (HR = 4.40, 95% CI [0.81–24.03], *p* = 0.087).

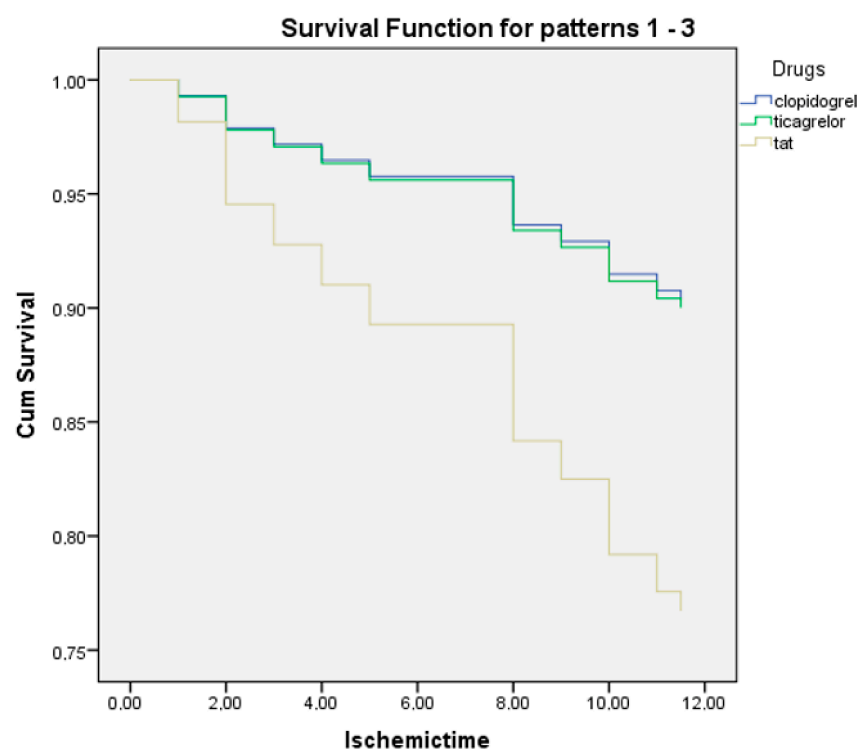


Figure 1. Cox regression analysis of 1-year survival outcomes regarding ischemic outcome, stratified by the antiplatelet agent used.

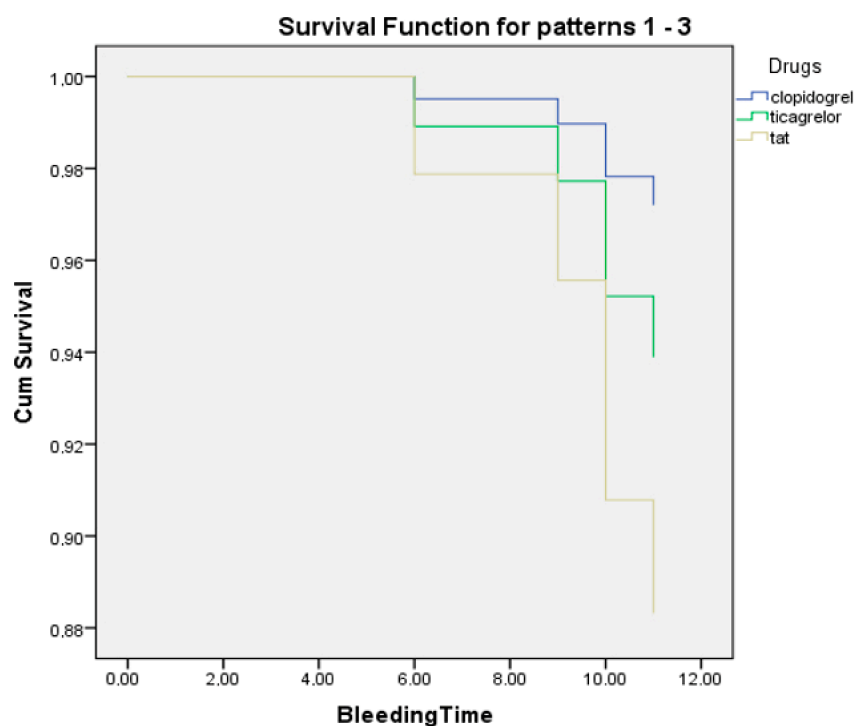


Figure 2. Cox regression analysis of 1-year survival outcomes regarding major bleeding outcome, stratified by the antiplatelet agent used.

5. Discussion

In this single-center, real-world cohort of non-valvular AF patients undergoing PCI for ACS, we observed no statistically significant differences between ticagrelor- and clopidogrel-based strategies for thromboembolic events or major bleeding, with a numerical excess of

minor bleeding under ticagrelor. Our grouping by the antiplatelet regimen used after a first-week blank period was intended to minimize bias from periprocedural complications and early treatment switches, thereby reflecting stable maintenance therapy choices.

The present study adds to a growing but still limited body of evidence on the optimal choice of P2Y₁₂ inhibitor in patients with atrial fibrillation (AF) undergoing PCI while receiving chronic oral anticoagulation (OAC). In this high-risk setting, the clinician is constantly balancing thromboembolic and ischemic risk against a substantial hazard of bleeding. Our findings, showing no clear ischemic advantage of ticagrelor over clopidogrel but a numerical excess of minor bleeding, are broadly aligned with contemporary evidence from meta-analyses and guideline-relevant trials.

Several quantitative syntheses have addressed the question of P2Y₁₂ inhibitor choice in anticoagulated AF-PCI patients. In a large meta-analysis including more than 22,000 participants, Lupercio et al. reported that ticagrelor and prasugrel were associated with significantly higher bleeding when combined with OAC compared with clopidogrel, with no reduction in major adverse cardiac events (MACE) [5]. Similarly, Casula et al. pooled randomized trials and demonstrated that potent P2Y₁₂ inhibitors increased major or clinically relevant non-major bleeding by approximately 30% relative to clopidogrel, again with no detectable benefit in MACE [6].

A nationwide Danish cohort by Godtfredsen et al. evaluated ticagrelor or prasugrel versus clopidogrel in AF patients undergoing PCI for MI. Ticagrelor/prasugrel was associated with a lower standardized risk of MACE at one year, while major bleeding did not differ significantly. Differences from meta-analytic findings may reflect residual confounding, high ischemic burden in MI populations, or selective use of potent P2Y₁₂ inhibitors in specialized centers [7]. Our study may provide evidence—albeit limited—indicating that potent P2Y₁₂ inhibitors can be used in patients with a high likelihood of a heavy ischemic burden, without the need to avoid them due to safety concerns (bleeding risk).

Pivotal DOAC-based trials consistently demonstrated less bleeding when aspirin is omitted and when DOACs replace VKAs, with broadly similar ischemic outcomes: PIONEER AF-PCI [7] (rivaroxaban strategies) reduced clinically significant bleeding versus VKA-based triple therapy without efficacy penalty; RE-DUAL PCI [8] (dabigatran dual therapy) lowered bleeding and was non-inferior for thromboembolic events versus warfarin-based triple therapy; and AUGUSTUS [9], using a 2 × 2 factorial design, showed less major/clinically relevant non-major bleeding with apixaban vs. VKA (HR ≈ 0.69) and with aspirin-placebo vs. aspirin (HR ≈ 1.89 for aspirin vs. placebo, indicating more bleeding with aspirin), with similar ischemic outcomes overall (death/hospitalization lower with apixaban).

In addition, in the ENTRUST-AF PCI [10] study, which included 1506 AF patients who underwent PCI, patients were investigated in 2 groups as Edoxaban and VKA, and while no significant difference was found in ischemic events, the group receiving Edoxaban was non-inferior bleeding.

Evidence from major DOAC-based randomized trials indirectly supports the preferential use of clopidogrel. In PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS, and ENTRUST-AF PCI, dual therapy (DOAC + single P2Y₁₂ inhibitor, predominantly clopidogrel) consistently reduced bleeding compared with VKA-based triple therapy while maintaining similar ischemic outcomes. Ticagrelor use in these trials was minimal, reflecting clinician caution regarding bleeding in anticoagulated patients [7–11].

ISAR-TRIPLE [12] tested the duration of clopidogrel within VKA-based triple therapy and found that 6-week vs. 6-month clopidogrel did not reduce ischemic events and did not significantly affect the composite endpoint, underscoring the bleeding liabilities of prolonged triple therapy. Finally, a contemporary meta-analysis [13] of DOAC-based dual

vs. triple therapy showed a ~34% relative reduction in major/CRNM bleeding with dual therapy but a higher risk of definite/probable stent thrombosis, while death, MI, stroke, and MACE were similar overall.

The 2023 ESC ACS Guidelines [3] recommend, for most AF-PCI patients, a DOAC plus a single P2Y12 inhibitor (preferably clopidogrel) with early aspirin discontinuation, emphasizing individualized balancing of ischemic and bleeding risk. Our real-world findings—no clear ischemic benefit of ticagrelor on top of OAC and a numerical increase in non-major bleeding—are concordant with this paradigm that prioritizes bleeding avoidance without sacrificing ischemic protection. When Jackson et al. (TRANSLATE-ACS study) compared clopidogrel and prasugrel in OAC + DAPT treatment in patients undergoing PCI after AMI, prasugrel use was found to have a numerical increase only in bleeding that did not require hospitalization compared to clopidogrel [14].

Mechanistically, this treatment paradigm is sound. Oral anticoagulants attenuate thrombin-mediated clot formation, which plays a major role in AF-related thrombosis. Once this pathway is effectively inhibited, the additional ischemic benefit from intensifying platelet inhibition is likely modest. Conversely, the bleeding penalty of combining OAC with a potent P2Y12 inhibitor is consistently demonstrated across data sets.

In the presence of therapeutic OAC, the incremental ischemic protection from intensifying P2Y12 blockade appears blunted, whereas the additive impact on bleeding remains substantial. Thus, a pragmatic default of DOAC plus clopidogrel after the first-week blank period seems reasonable for centers with a case mix similar to ours. Ticagrelor might be reserved for patients with very high thrombotic risk (e.g., prior stent thrombosis, complex PCI) after shared decision-making and close bleeding surveillance.

Overall, current evidence supports clopidogrel as the preferred P2Y12 inhibitor in AF patients requiring PCI and OAC. Ticagrelor may be considered only in highly selected patients with very high ischemic risk, such as those with prior stent thrombosis or extremely complex coronary anatomy. Future research should incorporate ARC-HBR criteria, procedural complexity, and pharmacogenomic profiling to refine individualized antithrombotic strategies.

6. Study Limitation

This study has several important limitations that should be acknowledged when interpreting the findings. First, although the study included consecutive real-world patients with atrial fibrillation undergoing PCI, the overall sample size was modest, and the distribution of patients among treatment groups was unbalanced. Particularly, the ticagrelor group and the triple therapy group comprised relatively small numbers of patients, substantially limiting statistical power. As a result, the absence of statistically significant differences should not be interpreted as evidence of therapeutic equivalence.

Secondly, the 1st week following PCI was excluded to minimize bias arising from the post-procedural sequence, subsequent events, and early changes in treatment. Although methodologically sound, this approach may have underestimated early differences between ticagrelor and clopidogrel, particularly during the period of high risk for acute stent thrombosis.

Third, the inclusion of a triple-therapy (ASA + clopidogrel + DOAC) group introduces clinical heterogeneity, as these patients differ inherently in risk profile and treatment strategy from those receiving dual therapy. Moreover, the small size of this group limits the interpretability of comparative findings.

Finally, this was a single-center, retrospective study, and the possibility of bias in patient selection, data recording, and outcome classification cannot be completely eliminated. Larger multicenter prospective studies with adjusted analyses are required to validate these findings and better determine whether any subgroup of anticoagulated AF-PCI patients may benefit more from ticagrelor than from clopidogrel.

7. Conclusions

In this retrospective real-world cohort of AF patients undergoing PCI for ACS, clopidogrel-based dual therapy appeared to provide clinical outcomes comparable to ticagrelor with respect to thromboembolic and bleeding events. No clear ischemic advantage of ticagrelor was observed, although a numerical increase in minor bleeding was noted. These observations are consistent with current guideline recommendations favoring DOAC-based dual therapy but should be considered hypothesis-generating because of the retrospective design, single-center setting, and limited sample size. Larger prospective multicenter studies are needed to confirm these findings and better define the optimal antithrombotic strategy in AF-PCI patients.

Author Contributions: F.S.Y. collected study data, wrote the main manuscript text and prepared figure and tables. A.A.B. applied statistics and reviewed the article. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Approval for our study was obtained from the ethics committee of İzmir Bakırçay University non-interventional clinical research with the decision number 2024/1872. Approved on 28 November 2024.

Informed Consent Statement: In this study, written informed consent was obtained from the patients who were followed up.

Data Availability Statement: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Steg, P.G.; Bhatt, D.L. Viewpoint: A proposal for a simple algorithm for managing oral anticoagulation and antiplatelet therapy in patients with non-valvular atrial fibrillation and coronary stents. *Eur. Heart J. Acute Cardiovasc. Care* **2017**, *6*, 93–97. [[CrossRef](#)] [[PubMed](#)]
2. Wang, T.Y.; Robinson, L.A.; Ou, F.-S.; Roe, M.T.; Ohman, E.M.; Gibler, W.B.; Smith, S.C.; Peterson, E.D.; Becker, R.C. Discharge antithrombotic strategies among patients with acute coronary syndrome previously on warfarin anticoagulation: Physician practice in the CRUSADE registry. *Am. Heart J.* **2008**, *155*, 361–368. [[CrossRef](#)] [[PubMed](#)]
3. Byrne, R.A.; Rossello, X.; Coughlan, J.J.; Barbato, E.; Berry, C.; Chieffo, A.; Claeys, M.J.; Dan, G.A.; Dweck, M.R.; Galbraith, M.; et al. ESC Guidelines for the management of acute coronary syndromes. *Eur. Heart J.* **2023**, *44*, 3720–3826, Erratum in *Eur. Heart J.* **2024**, *45*, 1145. [[CrossRef](#)] [[PubMed](#)]
4. Members, T.F.; Lip, G.Y.; Windecker, S.; Huber, K.; Kirchhof, P.; Marin, F.; Berg, J.M.T.; Haeusler, K.G.; Boriani, G.; Capodanno, D.; et al. Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: A joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). *Eur. Heart J.* **2014**, *35*, 3155–3179. [[CrossRef](#)] [[PubMed](#)]
5. Lupercio, F.; Giancaterino, S.; Villablanca, P.A.; Han, F.; Hoffmayer, K.; Ho, G.; Raissi, F.; Krummen, D.; Birgersdotter-Green, U.; Feld, G.; et al. P2Y12 inhibitors with oral anticoagulation for PCI with atrial fibrillation: Systematic review & meta-analysis. *Heart* **2020**, *106*, 575–583. [[CrossRef](#)] [[PubMed](#)]
6. Casula, M.; Fortuni, F.; Ferlini, M.; Fabris, F.; Oltrona Visconti, L.; Leonardi, S. Meta-Analysis Comparing Potent Oral P2Y12 Inhibitors versus Clopidogrel in Patients with Atrial Fibrillation Undergoing PCI. *Am. J. Cardiovasc. Drugs* **2021**, *21*, 231–240. [[PubMed](#)]
7. Gibson, C.M.; Mehran, R.; Bode, C.; Halperin, J.; Verheugt, F.W.; Wildgoose, P.; Birmingham, M.; Ianus, J.; Burton, P.; van Eickels, M.; et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N. Engl. J. Med.* **2016**, *375*, 2423–2434. [[CrossRef](#)] [[PubMed](#)]
8. Cannon, C.P.; Bhatt, D.L.; Oldgren, J.; Lip, G.Y.; Ellis, S.G.; Kimura, T.; Maeng, M.; Merkely, B.; Zeymer, U.; Gropper, S.; et al. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation (RE-DUAL PCI). *N. Engl. J. Med.* **2017**, *377*, 1513–1524. [[CrossRef](#)] [[PubMed](#)]

9. Lopes, R.D.; Heizer, G.; Aronson, R.; Vora, A.N.; Massaro, T.; Mehran, R.; Goodman, S.G.; Windecker, S.; Darius, H.; Li, J.; et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation (AUGUSTUS). *N. Engl. J. Med.* **2019**, *380*, 1509–1524. [[CrossRef](#)] [[PubMed](#)]
10. Vranckx, P.; Valgimigli, M.; Eckardt, L.; Tijssen, J.; Lewalter, T.; Gargiulo, G.; Batushkin, V.; Campo, G.; Lysak, Z.; Vakaliuk, I.; et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): A randomised, open-label, phase 3b trial. *Lancet* **2019**, *394*, 1335–1343. [[CrossRef](#)] [[PubMed](#)]
11. Martini, L.; Lisi, M.; Pompei, G.; Ariotti, M.; Bendandi, F.; Henein, M.Y.; Cameli, M.; Rubboli, A. Antiplatelet Therapy in Atrial Fibrillation Patients on Direct Oral Anticoagulants Undergoing Percutaneous Coronary Intervention: Which and How. *J. Clin. Med.* **2025**, *14*, 6331. [[CrossRef](#)] [[PubMed](#)]
12. Fiedler, K.A.; Maeng, M.; Mehilli, J.; Schulz-Schüpke, S.; Byrne, R.A.; Sibbing, D.; Hoppmann, P.; Schneider, S.; Fusaro, M.; Ott, I.; et al. Duration of triple therapy in patients requiring oral anticagulation after drug-eluting stent implantation: The ISAR-TRIPLÉ trial. *J. Am. Coll. Cardiol.* **2015**, *65*, 1619–1629. [[PubMed](#)]
13. Altoukhi, R.M.; Alshouimi, R.A.; Al Rammah, S.M.; Alzahrani, M.Y.; Almutairi, A.R.; Alshehri, A.M.; Alfayez, O.M.; Al Yami, M.S.; Almohammed, O.A. Safety and efficacy of dual versus triple antithrombotic therapy (DAT vs TAT) in patients with atrial fibrillation following a PCI: A systematic review and network meta-analysis. *BMJ Open* **2020**, *10*, e036138. [[CrossRef](#)] [[PubMed](#)]
14. Jackson, L.R.; Ju, C.; Zettler, M. Outcomes of patients with acute myocardial infarction undergoing percutaneous coronary intervention receiving an oral anticoagulant and dual antiplatelet therapy: A comparison of clopidogrel versus prasugrel from the TRANSLATE-ACS study. *J. Am. Coll. Cardiol. Interv.* **2015**, *8*, 1880.

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.