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Dual compared with triple antithrombotics treatment effect on ischemia and bleeding in atrial fibrillation following percutaneous coronary intervention: A meta-analysis

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Abstract

Background:
We performed a meta-analysis to evaluate the effects of dual antithrombotic treatment (DATT) including direct oral anticoagulants (OAs) versus triple antithrombotic (TAT) with vitamin K antagonist on bleeding and ischemic results in atrial fibrillation (AF) after percutaneous coronary intervention.

Methods:
A systematic literature search up to April 2021 was done and 5 studies included 8019 subjects with AF using antithrombotic treatment after percutaneous coronary intervention at the start of the study; 4325 of them were using DATT and 3694 were using TATs. They were reporting relationships between the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. We calculated the odds ratio (OR) with 95% confidence intervals (CIs) to assess the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention using the dichotomous method with a random or fixed-effect model.

Results:
Dual antithrombotics had significantly lower major bleeding (OR, 0.58; 95% CI, 0.51-0.66, p<0.001), and thrombolysis in myocardial infarction major and minor bleeding (OR, 0.49; 95% CI, 0.36-0.67, p<0.001) compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention.
However, antithrombotics had no significantly difference in all-cause mortality (OR, 1.08; 95% CI, 0.88-1.33, p=0.46), cardiovascular mortality (OR, 1.07; 95% CI, 0.83-1.38, p=0.63), myocardial infarction (OR, 1.16; 95% CI, 0.92-1.46, p=0.01), stent thrombosis (OR, 1.42; 95% CI, 0.94-2.12., p=0.09), and stroke (OR, 0.86; 95% CI, 0.59-1.25, p=0.42) compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention.

Conclusions:
Dual antithrombotics may have a lower risk of major bleeding, and thrombolysis in myocardial infarction major and minor bleeding compared to TATs in subjects with AF using antithrombotic treatment after percutaneous coronary intervention. However, antithrombotics had no significant difference in all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention. Furthers studies are required to validate these findings.

Keywords: dual antithrombotics; TATs; bleeding; ischemia; atrial fibrillation; percutaneous coronary intervention

Introduction

Revascularization by percutaneous coronary intervention is the standard of care for subjects with acute coronary syndrome. [1] Dual antiplatelet treatment, aspirin plus P2Y12 inhibitor, inhibits major adverse cardiovascular events after percutaneous coronary intervention in acute coronary syndrome or stable coronary artery disease. [1]

Though, about 10% of subjects experiencing percutaneous coronary intervention have atrial fibrillation (AF); which complicates the selection of optimal antithrombotic treatment. [2, 3] Direct oral antithrombotic agents are preferred over vitamin K antagonists in subjects with nonvalvular AF for better safety, lower bleeding, and efficiency in terms of major adverse cardiovascular events. [4] Randomized controlled trials compared other methods e.g. dual treatment comprising a direct oral antithrombotic and a P2Y12 inhibitor compared to triple treatment comprising a vitamin K antagonist and dual antiplatelet treatment, which was to recognize as an ideal antithrombotic strategy in subjects with AF after percutaneous coronary intervention. [5-9] Though, the cardiovascular aids gained by using triple treatment can be counterweight by the higher risk for bleeding. Also, the elimination of aspirin might cause higher rates of stent thrombosis and ischemic events with dual treatment. [10] This meta-analysis aimed to evaluate the effects of dual antithrombotic treatment (DATT) including direct oral anticoagulants (OAs) versus triple antithrombotic (TAT) with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention

Methods

The present study followed the meta-analysis of studies in the epidemiology statement, [11] which was performed following an established protocol.

Study selection

Included studies were that with statistical measures of association (odds ratio [OR], mean difference [MD], frequency rate ratio, or relative risk, with 95% confidence intervals [CIs]) between the effects of dual versus TATs treatment on bleeding and ischemic results in AF after percutaneous coronary intervention.

Only human research written in English were taken into consideration. No restrictions on inclusion were placed on study size or kind. Review articles, commentary, and research that did not provide a degree of association were publications that were omitted. Figure 1 depicts the entire course of the study.

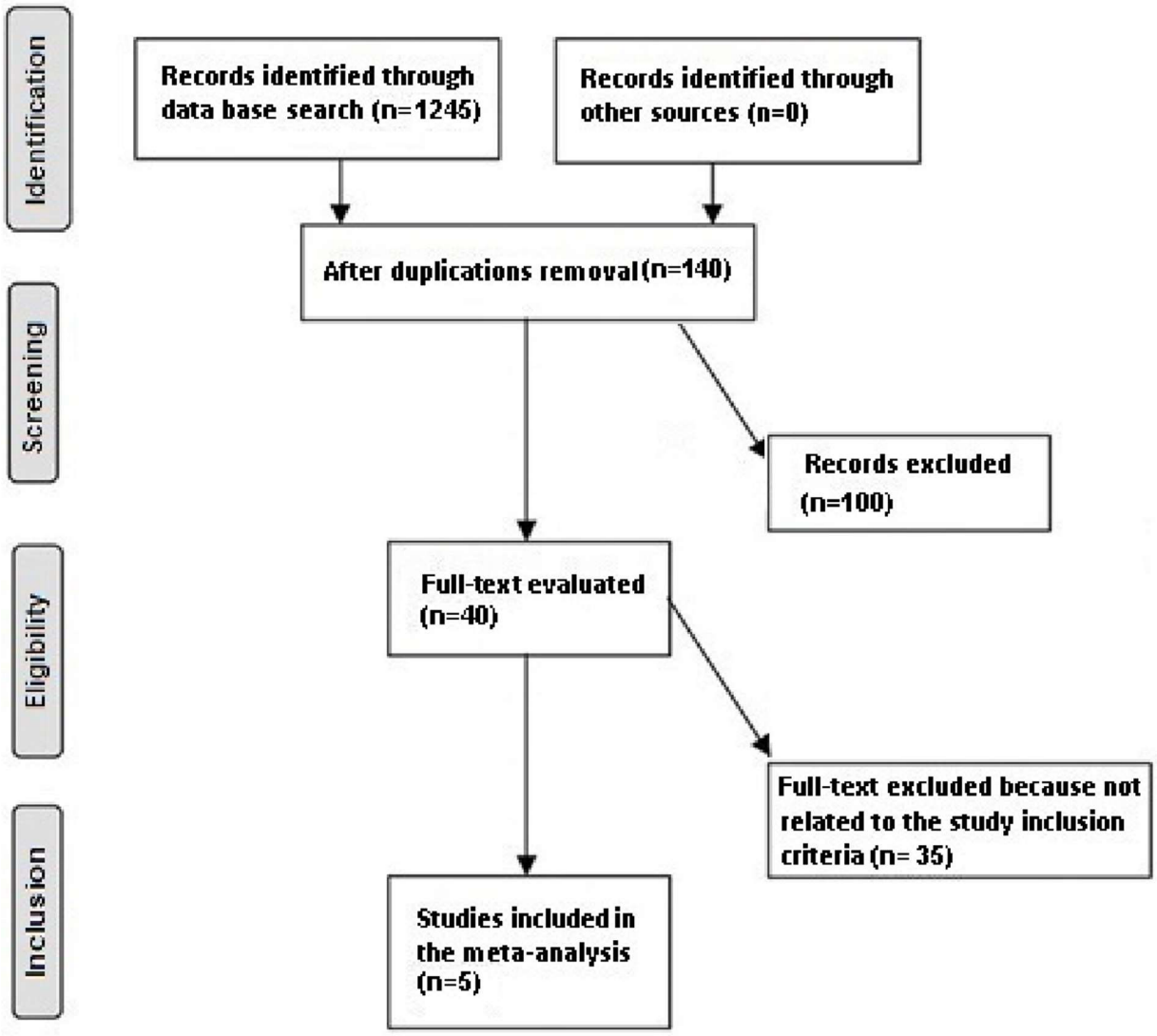

Figure 1. Schematic diagram of the study procedure The articles were integrated into the meta-analysis when the following inclusion criteria were met:

1. The study was a randomized control trial or retrospective study.
2. The target population is subjects with AF using antithrombotics treatment after percutaneous coronary intervention
3. The intervention program was antithrombotics
4. The study included comparisons between the dual and TATs treatment

The exclusion criteria for the intervention groups were:

1. Studies that did not determine effects of dual versus TATs treatment on bleeding and ischemic results in AF after percutaneous coronary intervention
2. Studies with treatments of AF after percutaneous coronary intervention other than antithrombotics
3. Studies did not focus on the effect of comparative results.

Identification

A protocol of search strategies was prepared according to the PICOS principle, [12] and we defined it as follow: P (population): subjects with AF using antithrombotics treatment after the percutaneous coronary intervention; I (intervention/exposure): antithrombotics; C (comparison): dual versus TATs treatment; O (outcome): change in the major bleeding, thrombolysis in myocardial infarction major and minor bleeding, all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke in subjects with AF using antithrombotics treatment after the percutaneous coronary intervention; and S (study design): no restriction. [13] First, we conducted a systematic search of Embase, PubMed, Cochrane Library, OVID, and Google scholar till April 2021, by a blend of keywords and related words for the dual antithrombotics, triple antithrombotics, bleeding, ischemia, atrial fibrillation, percutaneous coronary intervention as shown in Table 1. All detected studies were gathered in an EndNote file, duplicates were removed, and the title and abstracts were revised to eliminate studies that did not show any relationship between the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. The remaining studies were examined for related information.

Table 1. Search Strategy for Each Database

Database	Search strategy
Pubmed	#1 "dual anticoagulants"[MeSH Terms] OR "triple anticoagulants"[All Fields] OR "atrial fibrillation"[All Fields] #2 "ischemia"[MeSH Terms] OR "dual anticoagulants"[All Fields] OR "bleeding"[All Fields] OR "percutaneous coronary intervention"[All Fields] #3 #1 AND #2
Embase	'dual anticoagulants'/exp OR 'triple anticoagulants'/exp OR 'atrial fibrillation'/exp #2 'ischemia'/exp OR 'bleeding'/exp OR 'percutaneous coronary intervention'/exp #3 #1 AND #2
Cochrane library	#1 (dual anticoagulants):ti,ab,kw OR (triple anticoagulants):ti,ab,kw OR (atrial fibrillation):ti,ab,kw (Word variations have been searched) #2 (ischemia):ti,ab,kw OR (bleeding):ti,ab,kw OR (percutaneous coronary intervention):ti,ab,kw (Word variations have been searched) #3 #1 AND #2

Screening

The following properties of the study-related and subject-related data were condensed onto a standard form: Name of the primary author's last name, the duration of the study, the year it was published, the nation where the studies were conducted, and the study's design. Other information included the population type, the total number of subjects, demographic information, and clinical and treatment characteristics.[14] If a study met the criteria for inclusion in accordance with the aforementioned principles, data were independently retrieved by two writers. The corresponding author offered a deciding alternative in the event of a tie. When diverse study data were available, the assessment of the link between the effects was made of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention, we extracted them

separately. The risk of bias in these studies; individual studies were evaluated using two authors who independently assessed the methodological quality of the selected studies. The “risk of bias tool" from the RoB 2: A revised Cochrane risk-of-bias tool for randomized trials was used to assess methodological quality. [15] In terms of the assessment criteria, each study was rated and assigned to one of the following three risks of bias: low: if all quality criteria were met, the study was considered to have a low risk of bias; unclear: if one or more of the quality criteria were partially met or unclear, the study was considered to have a moderate risk of bias; or high: if one or more of the criteria were not met, or not included, the study was considered to have a high risk of bias. Any inconsistencies were addressed by a reevaluation of the original article.

Eligibility

The main result concentrated on the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. An assessment of the effects of dual versus TAT treatment on bleeding and ischemic results in AF after the percutaneous coronary intervention was extracted forming a summary.

Inclusion

Sensitivity analyses were limited only to studies reporting the relationship between the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. For subcategory and sensitivity analysis, we compared the dual and TATs treatment.

Statistical analysis

With either a random or fixed-effect model, we use the dichotomous technique to determine the odds ratio (OR) and 95% confidence interval (CI). We calculated the I2 index, and the range of the I2 index was 0% to 100%. When the I2 index was about 0%, 25%, 50%, and 75%, which, respectively, indicate no, low, moderate, and significant heterogeneity. [12] We employed the random-effect if the I2 was greater than 50% and the fixed-effect if it was less than 50%. To complete the subgroup analysis, we used stratification of the first assessment per outcome categories as previously mentioned. Statistical significance for differences between subcategories was defined as a p-value of less than 0.05. Publication bias was evaluated intuitively by looking at funnel plots of the logarithm of odds ratios vs their standard errors, and statistically by applying the Egger regression test (publication bias is present if p≥0.05).[14] The entire p-values were 2 tailed. Reviewer manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used to do all calculations and graphs.

Results

5 studies (between 2013 and 2021) that met the inclusion criteria and were found to be unique out of a total of 1245 research were included in the analysis. [5-9]

The 5 studies included 8019 subjects with AF using antithrombotic treatment after percutaneous coronary intervention at the start of the study; 4325 of them were using dual antithrombotics and 3694 were using TATs. All studies evaluated the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. In AUGUSTUS trial we used only 2 groups to simplify “Apixaban and placebo, and Vitamin K antagonist and aspirin”

The study size ranged from 581 to 2266 subjects with AF using antithrombotic treatment after percutaneous coronary intervention at the start of the study. The details of the 5 studies are shown in Table 2. The 5 studies reported data stratified to major bleeding, thrombolysis in myocardial infarction major and minor bleeding, all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke.

Dual antithrombotics had significantly lower major bleeding (OR, 0.58; 95% CI, 0.51-0.66, p<0.001) with low heterogeneity (I^2 = 33%), and thrombolysis in myocardial infarction major and minor bleeding (OR, 0.49; 95% CI, 0.36-0.67, p<0.001) with moderate heterogeneity (I^2 = 67%) compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention as shown in Figures 2 and 3.

However, antithrombotics had no significantly difference in all-cause mortality (OR, 1.08; 95% CI, 0.88-1.33, p=0.46) with no heterogeneity (I^2 = 0%), cardiovascular mortality (OR, 1.07; 95% CI, 0.83-1.38, p=0.63) with no heterogeneity (I^2 = 0%), myocardial infarction (OR, 1.16; 95% CI, 0.92-1.46, p=0.01) with no heterogeneity (I^2 = 0%), stent thrombosis (OR, 1.42; 95% CI, 0.94-2.12., p=0.09) with no heterogeneity (I^2 = 0%), and stroke (OR, 0.86; 95% CI, 0.59-1.25, p=0.42) with low heterogeneity (I^2 = 1%) compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention as shown in Figures 3-8.

Selected studies stratified analysis that adjusts for age, subject-level data, and ethnicity was not performed since no studies reported or adjusted for these factors. Only one study (RE-DUAL PCI) [9] had an update reporting data stratified analysis based on the gender and Apixaban dose given but we could not adjust for these factors because only RE-DUAL PCI stratified for these factors.

There was no indication of publication bias (p = 0.88) based on quantitative evaluation with the Egger regression test and visual inspection of the funnel plot. However, because of their substantial sample sizes, the majority of the included studies were judged to be of good methodological quality. As demonstrated in Figure 9, no studies had biassed selective reporting, and no articles had selective reporting and insufficient outcome data.

Table 2. Characteristics of the selected studies for the meta-analysis

Name	Study	Country	Total	Dual treatment	Triple treatment
WOEST	Dewilde, 2013 [5]	Multicenter	581	297	284
PIONEER	Gibson, 2016 [6]	Multicenter	1415	709	706
AUGUSTUS	Lopes, 2019 [7]	Multicenter	2266	1143	1123
ENTRUST-AF PCI	Vranckx, 2019 [8]	Multicenter	1506	751	755
RE-DUAL PCI	Eccleston, 2021 [9]	Multicenter	2251	1425	826
		Total	**8019**	**4325**	**3694**

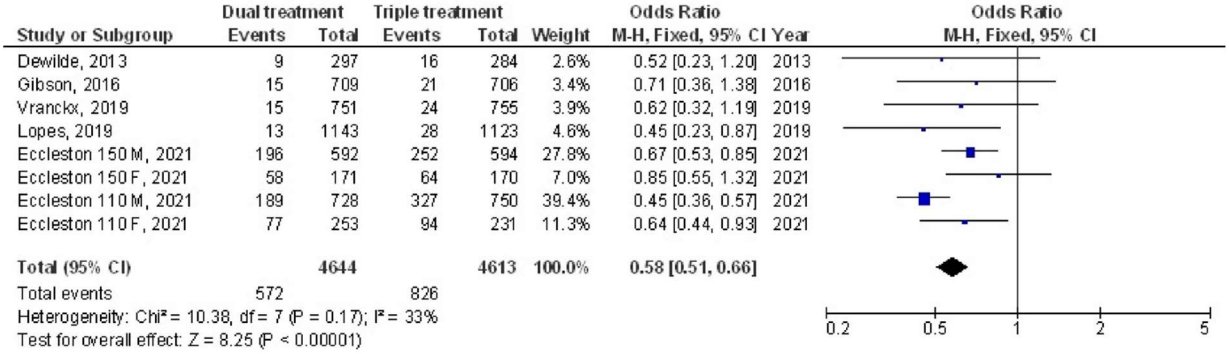

Figure 2. Forest plot of the prevalence of major bleeding in dual antithrombotics group compared to the triple antithrombotics group

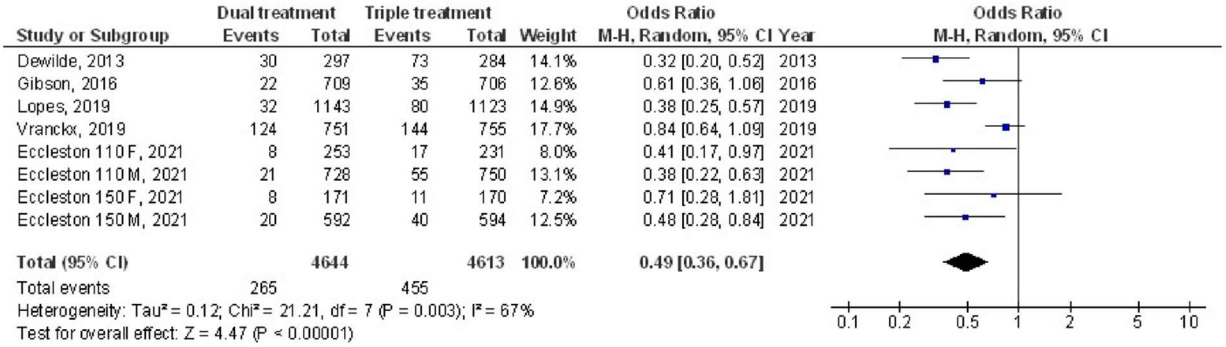

Figure 3. Forest plot of the prevalence of thrombolysis in myocardial infarction major and minor bleeding in dual antithrombotics group compared to the triple antithrombotics group

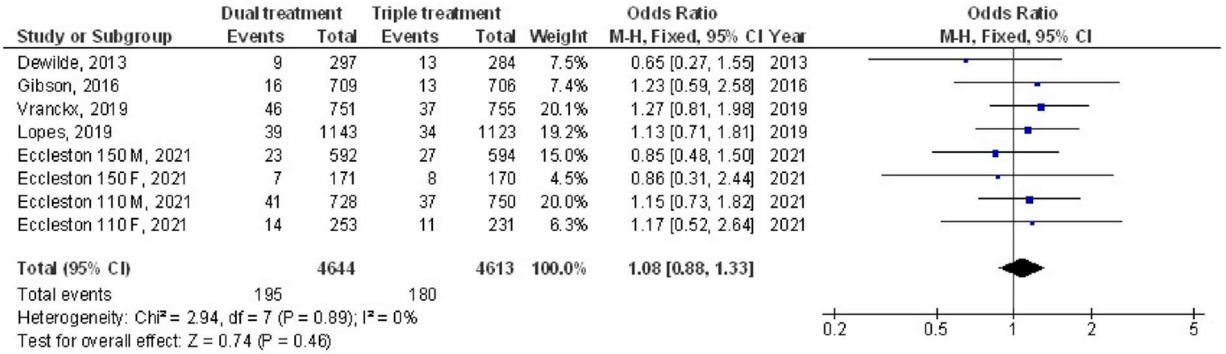

Figure 4. Forest plot of the prevalence of all-cause mortality in dual antithrombotics group compared to the triple antithrombotics group

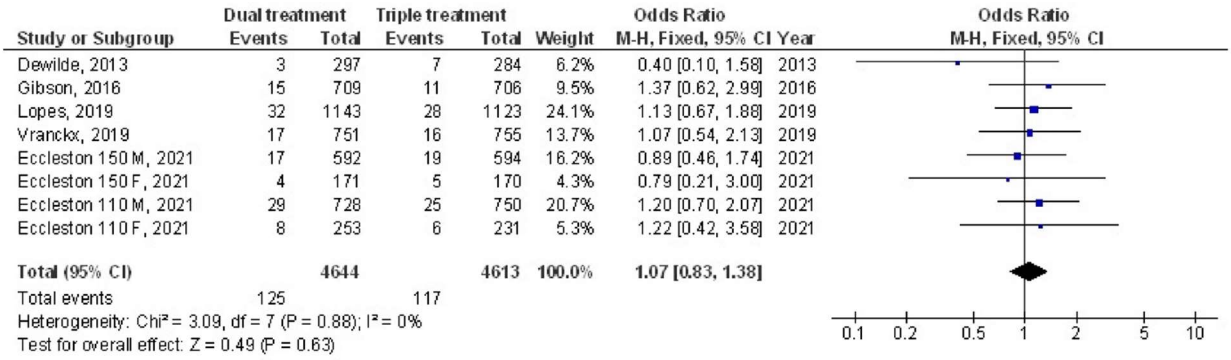

Figure 5. Forest plot of the prevalence of cardiovascular mortality in dual antithrombotics group compared to the triple antithrombotics group

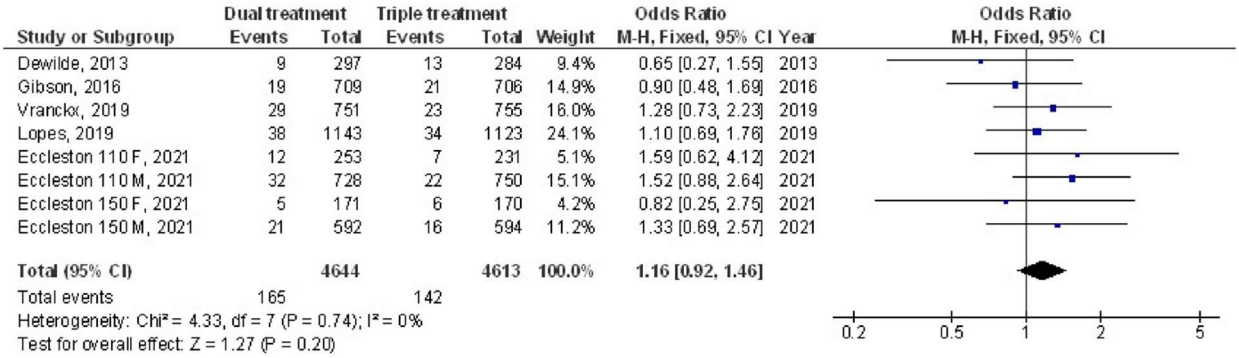

Figure 6. Forest plot of the prevalence of myocardial infarction in dual antithrombotics group compared to the triple antithrombotics group

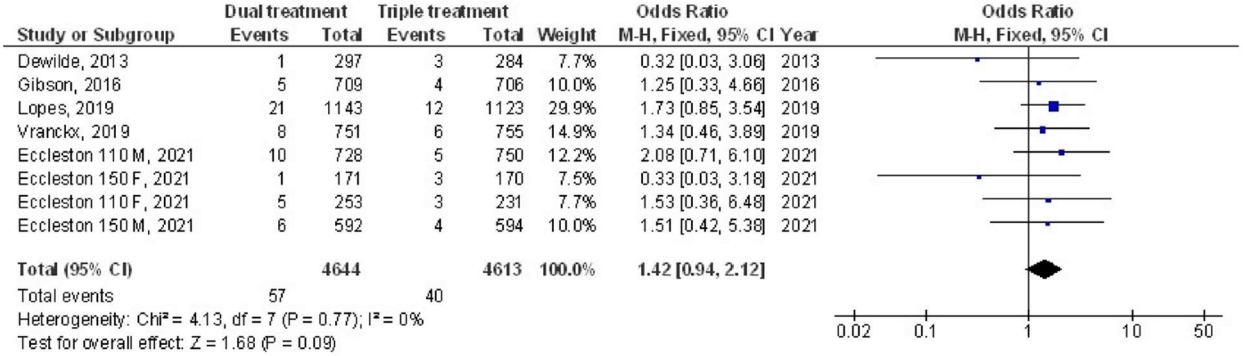

Figure 7. Forest plot of the prevalence of stent thrombosis in dual antithrombotics group compared to the triple antithrombotics group

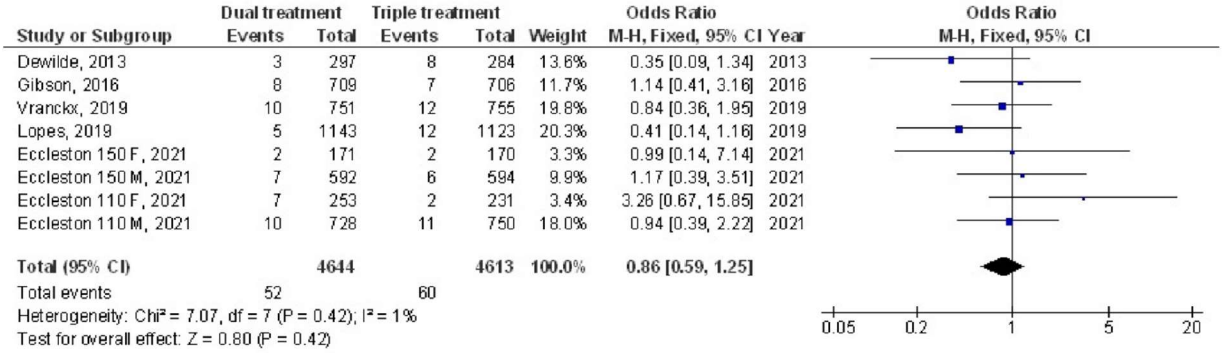

Figure 8. Forest plot of the prevalence of the stroke in dual antithrombotics group compared to the triple antithrombotics group

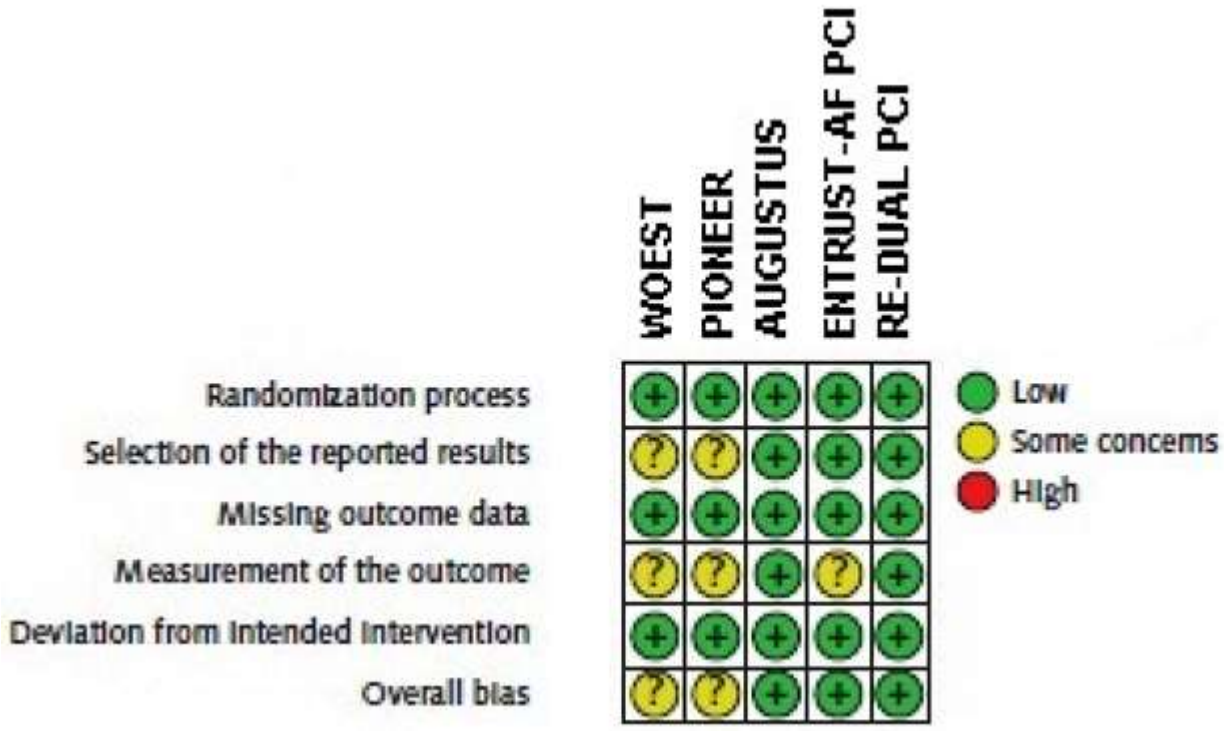

Figure 9. Risk of bias assessment

Discussion

This meta-analysis study based on 5 studies included 8019 subjects with AF using antithrombotic treatment after percutaneous coronary intervention at the start of the study; 4325 of them were using dual antithrombotics and 3694 were using TATs. [5-9] Dual antithrombotics had significantly lower major bleeding, and thrombolysis in myocardial infarction major and minor bleeding compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention.

However, antithrombotics had no significant difference in all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention. [5-9] However, due to the small number of studies included in our meta-analysis, it is advised to exercise caution while analysing the results, since this may have a major impact on the level of confidence in the effect evaluation e.g. stent thrombosis comparison with its relatively low p-value=0.09. The ongoing randomized controlled trials e.g. COACH-AF-percutaneous coronary intervention (Dabigatran vs. Warfarin With Nonvalvular AF Who Undergo percutaneous coronary intervention) (NCT03536611), APPROACH-acute coronary syndrome-AF (APixaban compared to. PhenpRocoumon in subjects With acute coronary syndrome and AF) (NCT02789917), OPTIMAL (Optimal Antithrombotic Therapy for acute coronary syndrome Patients Concomitant AF Undergoing New Generation Drug-Eluting Stent Implantation) (NCT03234114), and the Japanese S&E-A (Safety and Effectiveness Trial of Apixaban Use in Association With Dual antiplatelet therapy in Patients With AF Undergoing percutaneous coronary intervention) study, [16] will defiantly add to the finding.

In PIONEER, [6] rivaroxaban antithrombotic treatment indicated a lower risk for bleeding than triple treatment at 12 months. In RE-DUAL PCI [9, 17] at 14 months, triple treatment was related to a higher major or clinically relevant non-major bleeding compared to dabigatran. These findings were similar irrespective of index percutaneous coronary intervention subgroup, e.g. acute coronary syndrome or stable coronary artery disease, type of P2Y12 inhibitor treatment, or stent type. Those two studies did not explain whether the reduced bleeding risk with dual treatment was due to using a direct oral antithrombotic in place of a vitamin K antagonist or was because of an aspirin-free plan. [18] AUGUSTUS answered this question. [7] At 6 months, apixaban was related to a decrease in major or clinically relevant non-major bleeding compared with vitamin K antagonist; adding aspirin was related to an increase in bleeding versus placebo. [7] Opposing all aforementioned trials, ENTRUST-AF PCI had no significant differences for major or clinically relevant non-major bleeding events between dual treatment and triple treatment. [8] These findings could have been due to the lower bleeding rates in the vitamin K antagonist group throughout the first 2 weeks of management when a high proportion of subjects did not accomplish an international normalized ratio of 2. One of the previous meta-analyses had reported, [19] this might indeed be a potential explanation. A significant interaction was found at meta-regression analysis with the time with international normalized ratio below. Another potential explanation might be the different times to randomization among the studies, bringing to differences in the overlap between parenteral anticoagulants and/or oral aspirin and the experimental treatments in the studies. A

significant interaction was also reported between the effect size of bleeding complications and the time from index procedure to randomization. [19]

All randomized controlled trials demonstrate a numerical increase in ischemic endpoints with dual treatment. [5-9] The analysis of outcomes should be done with caution because of the limitations of each randomized controlled trial. In PIONEER the stent thrombosis endpoint was not centrally judged, and the directionality of efficiency endpoints was varying between antithrombotic groups. All dosing treatments of rivaroxaban, lower than 20-mg a day, were approved for stroke prevention in AF for subjects without significant renal impairment. [6] In RE-DUAL PCI, the composite efficiency endpoint was underpowered to distinguish clinical differences. [9, 17] A pooled analysis of both doses of dabigatran-based dual treatment in RE-DUAL PCI demonstrated an increase in the efficiency endpoint. [9, 17] In AUGUSTUS, myocardial infarction and stent thrombosis rates increased in subjects not getting aspirin. [7] However, low rates of event, insufficient power to evaluate cardiovascular results, and the limited follow-up period were the main limitations of this trial. [7] The treatment of AF after the percutaneous coronary intervention is a very common clinical mystery. The main queries are the aspirin withdrawal timing, whether aspirin treatment termination can result in any possible cardiovascular benefits, and the direct oral antithrombotic or vitamin K antagonist choice for oral anticoagulation. All comprised randomized controlled trials evaluated the safety of early aspirin withdrawal that is, before discharge from the hospital, as an explanation for the higher bleeding risk throughout the first month after percutaneous coronary intervention due to peri-procedural antithrombotic treatment.[5-9] A guideline from the American College of Cardiology, American Heart Association, and Heart Rhythm Society suggests restricting aspirin use in the pre-procedural time and through hospitalization. [20] Though, 2018 guidelines from the European Society of Cardiology limit the use of dual treatment only in subjects with a high risk of bleeding at baseline and suggest 1 to 6 months of triple treatment for all other subjects, based on thrombotic and risk of bleeding evaluation (class of suggestion, IIa for both guidelines). [1] These suggestions were made before the AUGUSTUS and ENTRUST-AF PCI trials. [7, 8] Generally, aspirin was considered the basis of the secondary prevention plans after percutaneous coronary intervention. [21] Though, a new model change favors P2Y12 inhibitor over aspirin after discontinuation of dual antiplatelet treatment. Recent studies compared an early de-escalation of dual antiplatelet treatment to P2Y12 inhibitor monotherapy (1 to 3 months) to 12 months of dual antiplatelet treatment. [22-25] These trials demonstrated better safety in bleeding events without deteriorating major adverse cardiovascular events. [22-25] Aspirin has very limited efficiency in preventing cardioembolic stroke especially in AF given the nature of thrombi that is less platelet mass than arterial thrombi. [21] Direct oral antithrombotics have demonstrated a more promising risk-benefit profile than vitamin K antagonists in AF. [26] AUGUSTUS showed that apixaban was related to lower death and hospitalization rates, due to the incident hospitalization rate and a relative risk decrease in stroke compared to vitamin K antagonist. [7] Current American and European guidelines favor direct oral antithrombotics over vitamin K antagonists for AF treatment in the lack of contraindications. [1, 20]

This meta-analysis showed the relationship between the effects of DATT including direct OAs versus TAT with vitamin K antagonist on bleeding and ischemic results in AF after percutaneous coronary intervention. However, further studies are needed to validate these potential relationships. Also, further studies are needed to deliver a clinically meaningful difference in the results. This was suggested also in previous similar meta-analysis studies which showed a similar effect of dual and TAT treatment in subjects with AF using antithrombotic treatment after percutaneous coronary intervention. [19, 27-43] However, The previous meta-analysis found an increased risk of stent thrombosis with specially dual antiplatelet treatment including a direct oral antagonists although results were obtained from the 3 first randomized controlled trial that were published. Those results make our analysis much more appropriate and our results, using all evidence currently available, clearly validate that direct oral Antagonist regimens do not increase the risk of stent thrombosis or, even more, cardiac ischemic events. [19, 27-43] Well-conducted studies are also needed to assess these factors and the combination of different subject-level data, age, and ethnicity; since our meta-analysis study could not answer whether they are associated with the results. Only one study (RE-DUAL PCI) [9] had an update reporting data stratified analysis based on the gender and Apixaban dose given. Similar updates are needed for the rest of the 4 studies since we could not adjust for these factors because only the update of RE-DUAL PCI stratified for these factors. In summary, dual antithrombotics may have a lower risk of major bleeding, and thrombolysis in myocardial infarction major and minor bleeding compared to TATs in subjects with AF using antithrombotic treatment after percutaneous coronary intervention. However, antithrombotics had no significant difference in all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention. Furthers studies are required to validate these findings.

Limitations

Since so many of the papers found in this study were not included in the meta-analysis, there may have been selection bias. The excluded papers, however, did not meet the requirements for inclusion in our meta-analysis. Additionally, we were unable to determine whether or not the results are related to subject-level data, age, and ethnicity. The study's goal was to determine the impacts of antithrombotics compared to TATs in subjects with AF using antithrombotics treatment after the percutaneous coronary intervention was based on data from previous studies, which might cause bias induced by incomplete details. The heterogeneity of all the studies included in the meta-analysis is relatively high. In AUGUSTUS, subjects were recruited and randomly allocated to a group within

14 days after an acute coronary syndrome or percutaneous coronary intervention. [7] Time to randomization was shorter in other trials. In RE-DUAL PCI, aspirin treatment was terminated after 1 month in subjects with a bare-metal stent or after 3 months in subjects with a drug-eluting stent. [9, 17] In PIONEER, subjects received dual antiplatelet treatment for 1, 6, or 12 months. [6] Since we relied on trial-level data, we could not examine outcomes based on direct oral antithrombotic type, P2Y12 inhibitor type, age, or comorbid conditions. Clopidogrel was used in over 90% of study participants. Therefore, we could not evaluate the effect of different P2Y12 inhibitors on the results. In all randomized controlled trials, lower rates of ischemia were found than expected, resulting in restricted statistical power to identify significant differences among groups in ischemia and death results. All randomized controlled trials excluded subjects with renal dysfunction and recruited subjects with comparatively low bleeding risk, limiting the generalizability of their findings. The open-label design of the trials might bias the outcomes in favor of dual treatment. The compliance, subject-level data, age, ethnicity, and nutritional health of the subjects were all variables that could introduce bias. Some unpublished articles and missing data could cause the pooled effect to be biassed. Different therapy regimens, doses, and medical systems were applied by the subjects.

Conclusions

Dual antithrombotics may have a lower risk of major bleeding, and thrombolysis in myocardial infarction major and minor bleeding compared to TATs in subjects with AF using antithrombotic treatment after percutaneous coronary intervention. However, antithrombotics had no significant difference in all-cause mortality, cardiovascular mortality, myocardial infarction, stent thrombosis, and stroke compared to TATs in subjects with AF using antithrombotics treatment after percutaneous coronary intervention. Additional research is necessary to verify these findings. However, due to the small number of studies included in our meta-analysis, it is advised to exercise caution when analysing the results, as this may indicate the need for additional research to confirm these results or perhaps have a substantial impact on confidence in the effect assessment.

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