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RESEARCH

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# A comparison of the effects of ticagrelor and clopidogrel in patients with acute ST-segment elevation myocardial infarction: a systematic review and meta-analysis of randomized clinical trials

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## Abstract

**Background** Rupture of unstable coronary atherosclerotic plaque leads to acute ST-segment elevation myocardial infarction (STEMI). Dual anti-platelet therapy is one of the main treatments, and the combination of Aspirin and Clopidogrel is recognized as the standard oral regimen in most cases. Ticagrelor is a new generation of P2Y12 receptor inhibitors. We aimed to compare the effect of Ticagrelor and Clopidogrel in the treatment of patients post-STEMI.

**Methods** This study investigated Pub Med, Scopus, Google Scholar Web of Science, and Embase Cochrane Library clinical trials.gov databases. Heterogeneity between studies was assessed using the I2 index and the Q statistic. The random effects model was used to combine studies and the Funnel plot and Egger's test were used to assess the publication bias.

**Results** Eleven studies were included in this meta-analysis. 5274 patients in the Ticagrelor and 5,295 patients in the Clopidogrel groups were examined. The mean age of the patients was 58.84 years (2.70) and 59.92 years (3.19) in the Ticagrelor and Clopidogrel groups, respectively. Based on the results of the meta-analysis, compared to Clopidogrel, Ticagrelor had decreased the outcomes of mortality, recurrent myocardial infarction, stroke, and Major Adverse Cardiovascular Events (MACE). However, the post-myocardial infarction bleeding according to Bleeding Academic Research Consortium (BARC) criteria and reperfusion state regarding thrombolysis in myocardial infarction (TIMI) Flow Grading system showed no differences in both groups. However, these effects were not statistically significant.

**Conclusions** Ticagrelor decreased the chance of mortality, re-infarction, stroke, and MACE in post-STEMI patients compared to clopidogrel. But there was no difference in the chance of major bleedings (BARC ≥ 3) and improvement in TIMI grade flow between these two drugs. However, none of these findings were statistically significant, and more studies are needed to reach definitive results.

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**Keywords** Acute coronary syndrome, Ticagrelor, Clopidogrel, Anti-platelet

## Background

Acute Coronary Syndrome (ACS) is a clinical syndrome that includes unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Among these, acute STEMI is the most critical type of ACS, characterized by poor prognosis, rapid onset, dangerous progression, and high mortality rate. Rupture of unstable coronary atherosclerotic plaque, which causes thrombosis, myocardial infarction (MI), and even necrosis, leads to acute STEMI. Therefore, the opening of the Infarct-Related Artery (IRA), which restores the ischemic myocardium and reperfuse the vessel, successfully treats acute STEMI [1]. Therapy in STEMI patients can be pursued with two strategies, primary percutaneous coronary intervention (PPCI) and aggressive Pharmacological Interventions (PI) [2]. PIs are defined as the early administration of fibrinolytic therapy followed by Percutaneous Coronary Intervention (PCI) [3]. Although, according to clinical guidelines, PPCI is the preferred reperfusion method chosen for these patients, fibrinolytic therapy is the first line of treatment in situations where timely treatment of the patient with PPCI is not possible [1, 4].

Antiplatelet therapy is an essential part of the treatment regimen of patients with acute MI, and the importance of dual antiplatelet therapy in the treatment of STEMI patients has been acknowledged [5–7]. The combination of Aspirin and Clopidogrel is recognized as the standard oral antiplatelet regimen in ACS. However, the antiplatelet effect of Clopidogrel requires sequential and time-consuming metabolic steps, which leads to a delay in achieving platelet inhibition. In addition, a tiny proportion of patients are genetically resistant to Clopidogrel, and the level of response to this agent can be somewhat unpredictable. These disadvantages of Clopidogrel have led to the development of more potent and faster antiplatelet drugs such as Ticagrelor [8–10]. Ticagrelor has been introduced as a new generation of P2Y12 receptor inhibitors, which is a direct P2Y12 receptor antagonist [11, 12]. Although the superiority of Ticagrelor's clinical efficacy has been shown in various studies, issues related to its side effects, such as the risk of major bleeding, which increases the mortality rate, require further investigation [4, 13–15]. This present study aims at performing a meta-analysis of Randomized Clinical Trial (RCT) studies to compare the effects of Ticagrelor and Clopidogrel in STEMI patients.

## Methods

This systematic meta-analysis was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [16].

### Data sources

A systematic review of published studies was conducted to compare the efficacy of Clopidogrel and Ticagrelor in patients with STEMI. For this purpose, the databases PubMed, Scopus, Web of Science, Embase, Cochrane Library, and clinical trials.gov were searched using the logical combination of keywords and their MeSH terms, including, Ticagrelor, Clopidogrel, ST-segment elevation myocardial infarction, P2Y12 inhibitors, and antiplatelet therapy. This search was conducted until the end of June 2022. The PubMed search strategy is provided in Table 1.

### Selection criteria and data extraction

Randomized Clinical Trial (RCT) studies published in English and compared antiplatelet therapy with Ticagrelor and Clopidogrel in STEMI patients were included in this study. Studies whose full text was not available were excluded. In case of overlapping research data, such as information from the same RCT published in multiple articles, the most completed and up-to-date report was selected for inclusion in the meta-analysis. For further clarification, direct contact with authors was initiated for cases with either vague or incomplete information. In addition, an identical search strategy was adopted in other databases, and the key journals and reference lists of the presented articles were also searched. Finally, searches were combined using Endnote X5.

The following inclusion criteria were considered for the review of articles: (1) Randomized clinical trial studies (RCT), (2) Articles published in English, whose full text was available, (3) Studies conducted on human subjects over 18 years of age, and (4) Studies comparing antiplatelet treatment with Ticagrelor and Clopidogrel in STEMI patients. The exclusion criteria included the following: (1) studies that examined patients with comorbidity, (2) studies that provided incomplete information about the intended outcomes of the study, and (3) studies that had a design other than RCT and were written in a language other than English.

The researchers extracted the information from the articles in Excel form. This information included the bibliographic information of the articles (title, authors, year of publication, country, TRIAL registry number), patient characteristics (sample size, age, sex ratio of each gender), drug characteristics (dose, follow-up, number of patients in each arm of the study, loading dose and maintenance dose) and information about the outcomes of the study (mortality, stroke, MI, Major Adverse Cardiovascular Events (MACE), Bleeding academic research consortium (BARC) score, and Thrombolysis in myocardial infarction (TIMI) Flow Grade.)

**Table 1** PubMed search strategy

| | |
|---|---|
| #1 | (STEMI [Title/Abstract] OR "Myocardial Infarction" [Title/Abstract] OR "st elevation myocardial infarction" [Title/Abstract] OR "ST segment elevation myocardial infarction" [Title/Abstract]) OR ("ST Elevation Myocardial Infarction" [Mesh]) |
| #2 | (clopidogrel [Title/Abstract] OR iscover [Title/Abstract] OR "pcr 4099" [Title/Abstract] OR "sr 25989" [Title/Abstract] OR "sr 25990c" [Title/Abstract] OR sr25990c [Title/Abstract] OR plavix [Title/Abstract]) OR ("Clopidogrel" [Mesh]) |
| #3 | (ticagrelor * [Title/Abstract] OR Brilique * [Title/Abstract] OR Possia * [Title/Abstract] OR AZD6140 [Title/Abstract] OR AZD 6140 [Title/Abstract] OR 274693-27-5 [Title/Abstract] OR GLH0314RVC [Title/Abstract]) OR ("Ticagrelor" [Mesh]) |
| #4 | (#2 AND #3) AND #1 |

#### Major adverse cardiovascular events (MACE)

MACE is the sum of outcomes such as re-hospitalization due to heart failure (HF), total death, MI, stroke, and revascularization, including percutaneous interventions and surgical bypass grafts [17].

#### Bleeding academic research consortium (BARC) score

New advances in treating ACS, including prescription dual antiplatelet therapies and anticoagulants simultaneously, as well as revascularization methods such as thrombolytics and invasive trans-arterial revascularization methods, have lowered the risk of mortality and many other adverse effects post-MI. However, they significantly increase the risk of major bleeding. To evaluate the safety of antithrombotic treatments in clinical trials regarding the risk of bleeding, academic research consortium (BARC) criteria were defined in February 2010. The BARC criteria divided the post-MI bleeding into five types, from 0: no bleeding to 5: fetal bleeding [18].

#### Thrombolysis in myocardial infarction (TIMI) flow grade

Thrombolysis in myocardial infarction (TIMI) criteria is defined by the contrast flow rate assessed visually during coronary angiography before and after treatment, and it has been proven to have prognostic information in post-MI patients. The criteria were first introduced in 1984 and consisted of 3 stages: stage 0: no antegrade flow to stage 3: which shows normal flow distal to the coronary artery lesion [19].

The Standard Cochrane Collaboration risk of bias tool checklist in *Revman 5.3* software was used to evaluate the methodology of the included articles. Also, the GRADE (The Grading of Recommendation Assessment, Development, and Evaluation) tool was used to check the quality of the evidence obtained from the meta-analyzer. All steps of the search, selection of studies, data extraction, and quality assessment were carried out by two independent authors. If there were any differences, they were resolved by discussion until reaching a consensus or by consulting the third author.

#### Statistical analysis

The number of occurrences for each outcome was extracted along with the sample size of the articles. I2 index and Q statistic were used to check the lack of homogeneity between studies. An I2 value greater than 50% was considered as the presence of inhomogeneity. Random effects model using the Mantel-Haenszel method was used to combine studies, and the Risk Ratio was calculated. Finally, funnel Plot and Egger's tests were used to check the publication bias. A probability value of less than 5% was considered a significant level. The meta package available in R software version 4.2.1 was used for data analysis.

#### Search results and study characteristics

The present meta-analysis study involved a rigorous search of multiple sources, identifying 6912 articles. Of these, 2832 were determined to be duplicates and excluded from further consideration. An additional 4037 articles were excluded after thoroughly examining their respective titles and abstracts. Finally, the full texts of the remaining 43 articles were carefully reviewed, excluding a further 32 articles. Ultimately, 11 articles were found to meet the pre-defined inclusion criteria and were included in the present meta-analysis. A detailed flowchart depicting the article identification and selection process is presented in Fig. (1).

## Results

Eleven studies were included in the meta-analysis. Five thousand two hundred seventy-four participants in the ticagrelor group and 5295 participants in the clopidogrel group were examined [4, 6, 13, 20–26].

In the quality assessment results of this study, five of the studies were OPEN LABEL [4, 14, 20, 24, 26], and one study did not provide information regarding the randomization process and blinding [21]. Overall, none of the studies clearly explained the blinding of outcome assessment. Therefore, it may cause detection bias (Figs. 2 and 3).

#### Meta-analysis results

The mean (standard deviation) ages of patients in the ticagrelor group and the clopidogrel group were 58.84 years (2.70) and 59.92 years (3.19), respectively. Eight hundred seventy-three patients in the ticagrelor group (16.55%) and 882 patients in the clopidogrel group (16.65%) had diabetes.

#### Mortality

In 6 studies, deaths were reported in two groups of patients with the causes of death in these 6 studies as follows:

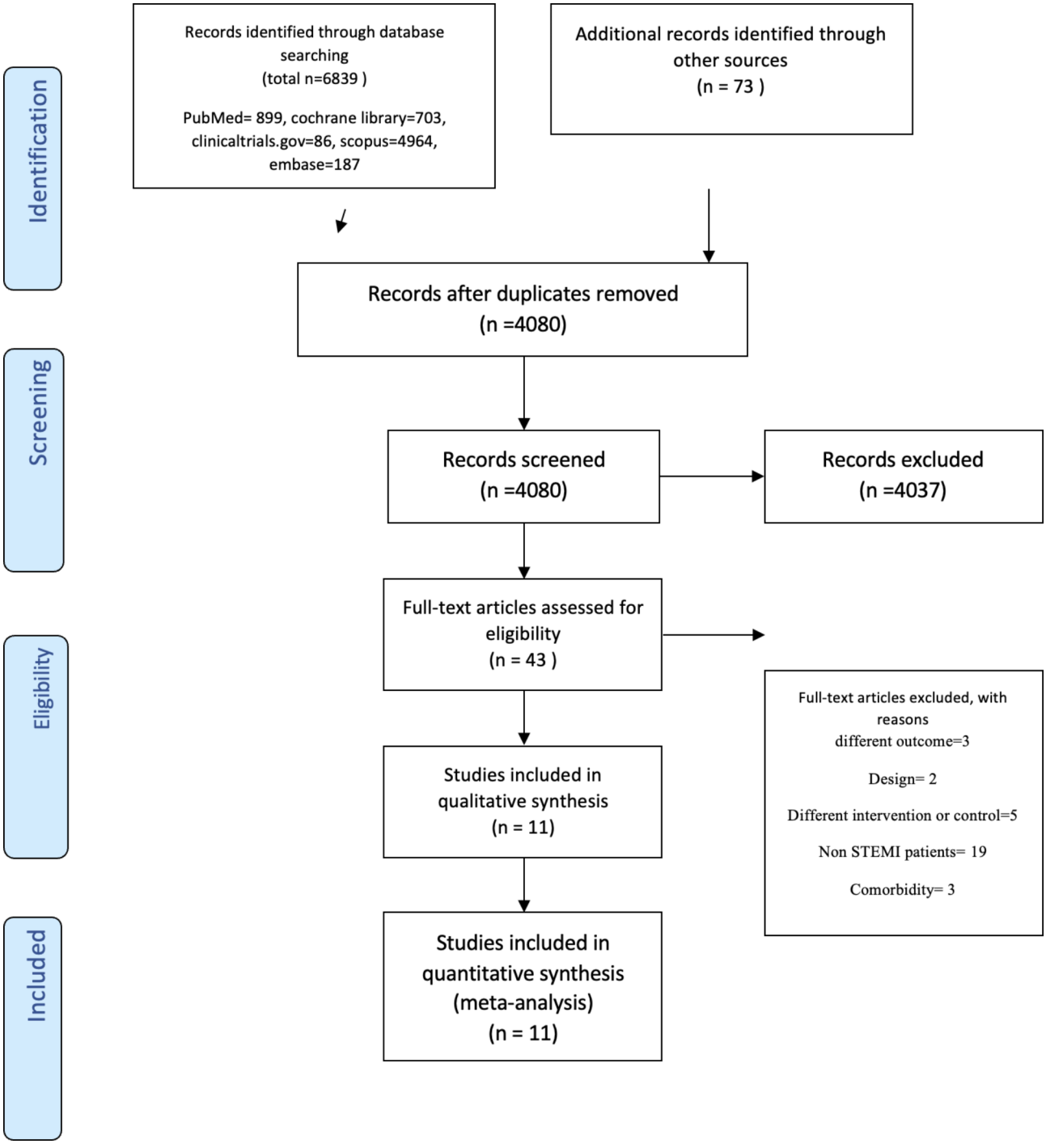


**Fig. 1** Prisma flow diagram for clinical trials

1. In-hospital deaths, including fatal bleeding.
2. All-cause deaths.
3. Three deaths in the Clopidogrel group: one related to catheter-induced perforation of the iliac artery, and two sudden cardiac deaths on days 4 and 5 post-PCI. In the Ticagrelor group, one patient died within an hour of a successful PCI, though no autopsy was performed.
4. Cardiac death.
5. Death from vascular causes, MI, or non-hemorrhagic stroke
6. Unspecified deaths

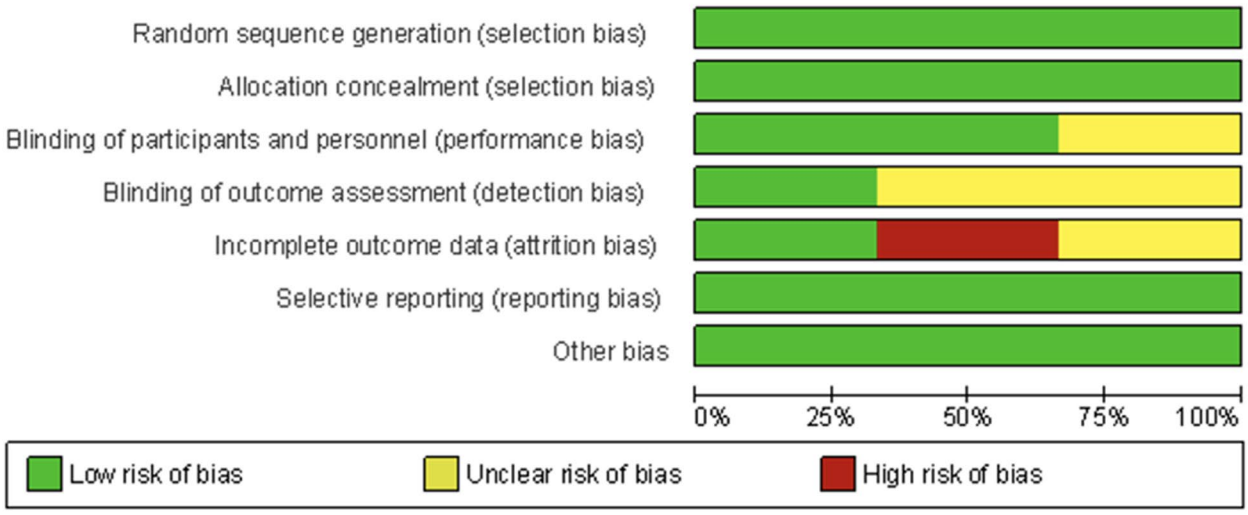


**Fig. 2** Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies

The number of patients in the Ticagrelor and Clopidogrel groups was 2,480 and 2,443, respectively. Also, the number of deaths observed in the Ticagrelor and Clopidogrel groups was 78 and 91, respectively. Based on the meta-analysis results, the risk ratio of death in the ticagrelor group was 0.86 more than that of the clopidogrel group, which was not statistically significant (RR=0.857, 95% CI = (0.637–1.153), z-value=-1.02, p-value=0.31). The forest plot related to the combination of results is shown in Fig. 4.

#### Ischemic stroke

In 5 studies, stroke rates were reported in two patient groups. The number of patients in the Ticagrelor and Clopidogrel groups was 2,312 and 2,276, respectively. Also, the prevalence of stroke amongst the Ticagrelor and Clopidogrel groups was 29 and 36, respectively. Based on the meta-analysis results, the Risk Ratio for Stroke in the ticagrelor group was 0.83 more than that of the clopidogrel group, which was not statistically significant (RR=0.83, 95% CI = (0.508–1.348), z-value=-0.76, p-value=0.45). The forest plot related to the combination of results is shown in Fig. 5 [27].

#### Recurrent myocardial infarction (re-MI)

In 6 studies, Recurrent MI was reported in two groups of patients. The number of patients in the Ticagrelor and clopidogrel groups was 2467 and 2470. The number of recurrent MI observed in the Ticagrelor and Clopidogrel groups was 49 and 58. Based on the meta-analysis results, the Risk Ratio for MI in the Ticagrelor group was 0.68 more than that of the Clopidogrel group, which was not statistically significant (RR=0.68, 95% CI = (0.333–1.382), z-value=-1.07, p-value=0.28). The forest plot related to the combination of results is shown in Fig. 6.

#### MACE: major adverse cardiovascular events

In 4 studies, MACE was reported in two groups of patients. The number of patients in the ticagrelor and clopidogrel groups was 457 and 488, respectively. Also, the incidence of MACE observed in the Ticagrelor and Clopidogrel groups was 10 and 20. Based on the meta-analysis results, the Risk Ratio for MACE in the ticagrelor group was 0.63 more than that of the clopidogrel group, which was not statistically significant (RR=0.63, 95% CI = (0.226–1.75), z-value=-0.89, p-value=0.37). The forest plot related to the combination of results is shown in Fig. 7.

#### Bleeding academic research consortium (BARC) criteria

In 7 studies, BARC scores were reported in two groups of patients. The number of patients in the Ticagrelor and Clopidogrel groups was 2,635 and 2,637. The number of BARC scores equal and more than 3 (BARC≥3), defined by overt bleeding causing hemoglobin drop or intracranial hemorrhage, observed in the Ticagrelor and Clopidogrel groups was 48 and 48, respectively. Based on the results of the meta-analysis, the Risk Ratio for BARC≥3 in the Ticagrelor group was 1.02 times more than that of the Clopidogrel group, which was not statistically significant (RR=1.02, 95% CI = (0.651–1.595), z-value=0.08, p-value=0.93). The forest plot related to the combination of results is shown in Fig. 8.

#### Thrombolysis in myocardial infarction (TIMI) flow grade

In 5 studies, TIMI Flow Grade was reported according to angiographic findings in two groups of patients. The

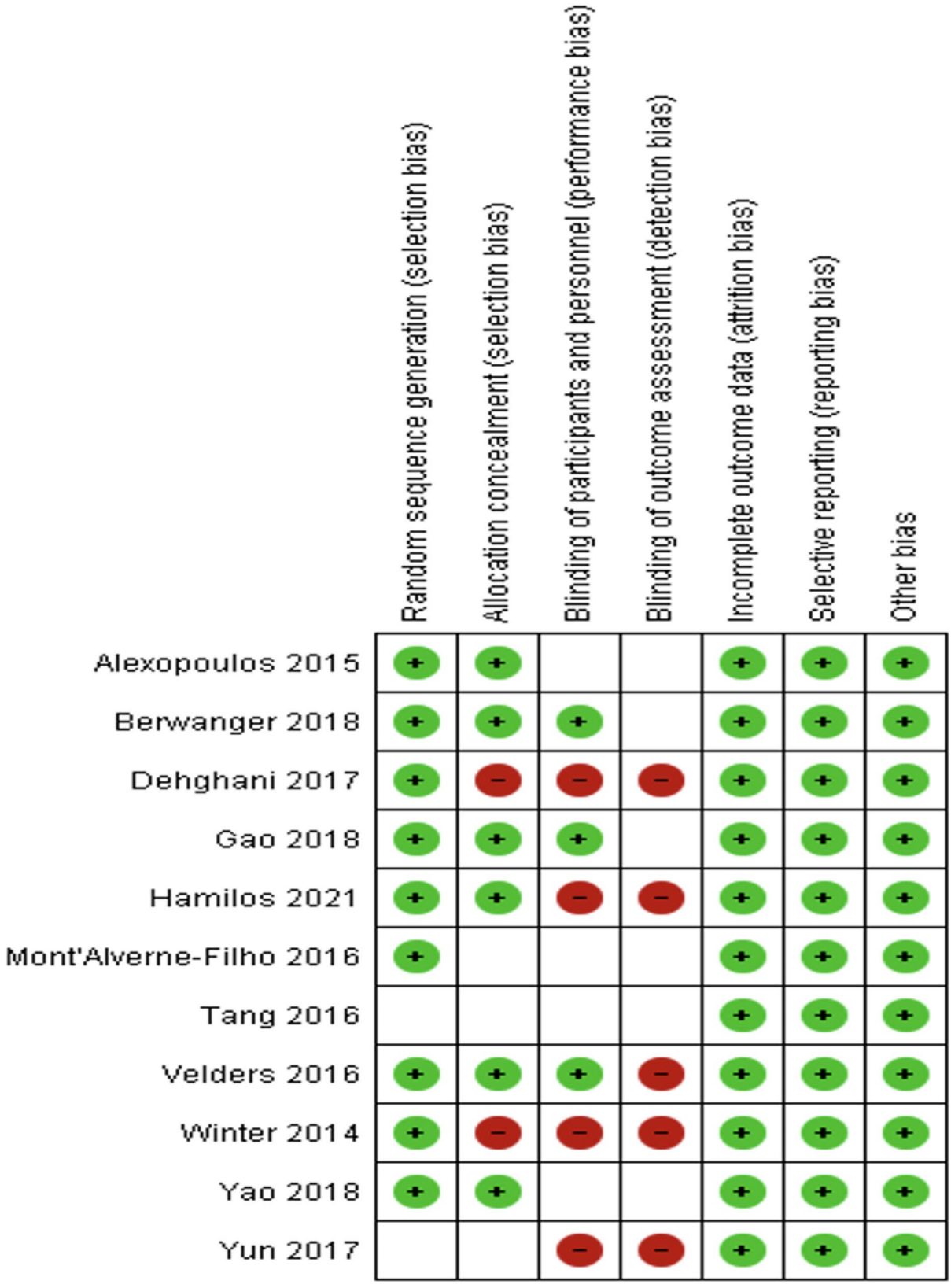


**Fig. 3** Risk of bias summery: review authors' judgments about each risk of bias item for each included study

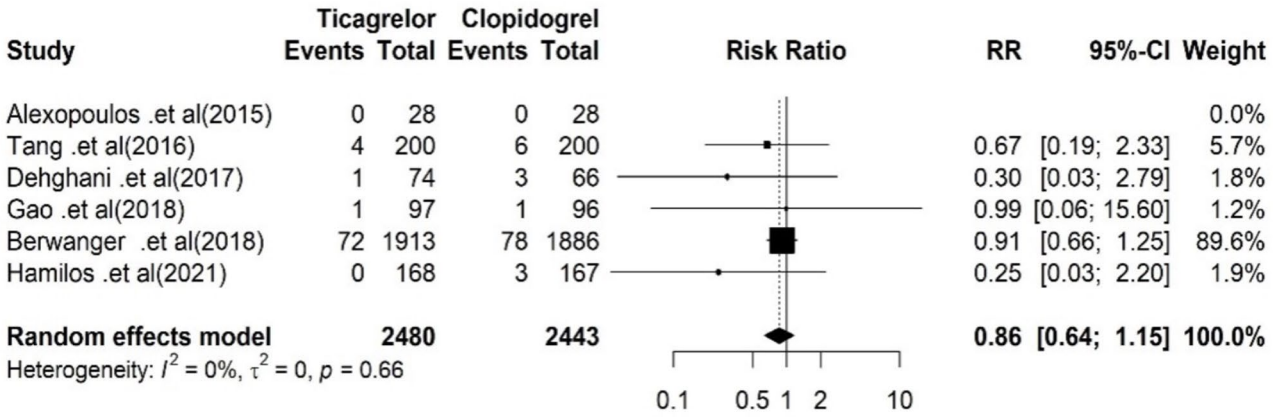


**Fig. 4** The mortality rate in Ticagrelor and Clopidogrel groups

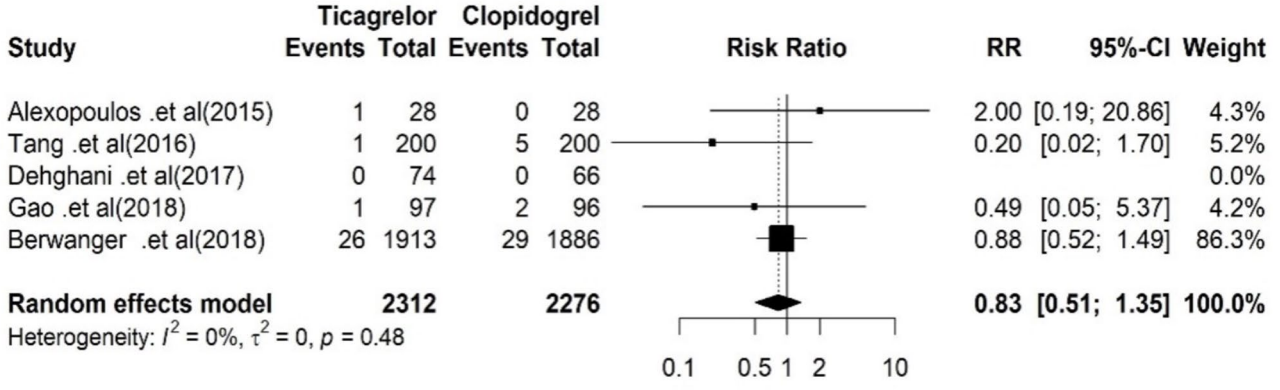


**Fig. 5** Stroke rate in Ticagrelor and Clopidogrel groups

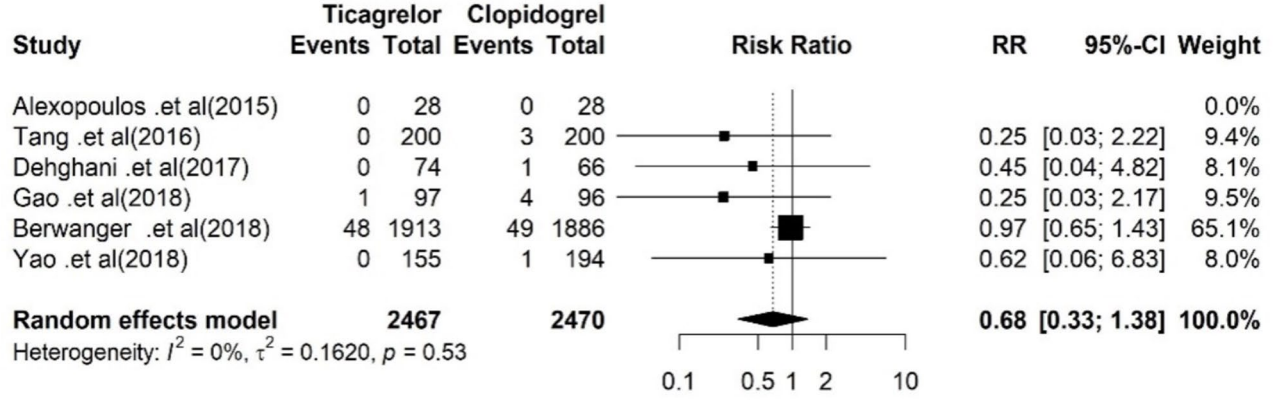


**Fig. 6** Recurrent myocardial infarction in Ticagrelor and Clopidogrel groups

number of patients in the Ticagrelor and Clopidogrel groups was 2,067 and 2,032, respectively. An increase in TIMI Flow Grade was reported in the 135 and 130 participants of the Ticagrelor and Clopidogrel groups. Based on the results of the meta-analysis, the Risk Ratio for an increase in the TIMI Flow Grade amongst the ticagrelor group was 1.02 more than that of the clopidogrel group, which was not statistically significant (RR=1.02, 95% CI = (0.86–1.201), z-value=0.19, p- value=0.85). The forest plot related to the combination of results is shown in Fig. 9.

### Publication bias

To assess the publication bias and Egger test results, Funnel plots related to each result are shown in Fig. 10. Egger's test was significant for recurrent MI outcomes

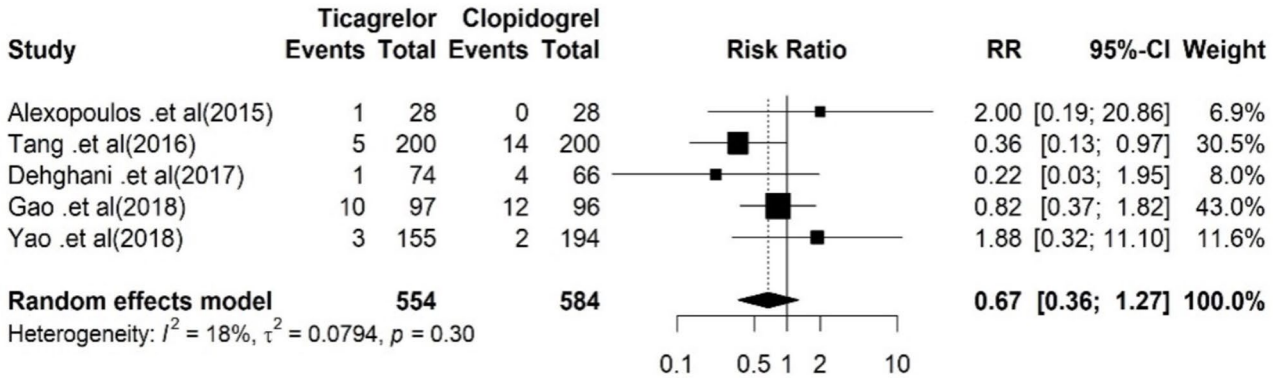


**Fig. 7** Major Adverse Cardiovascular Events in Ticagrelor and Clopidogrel groups

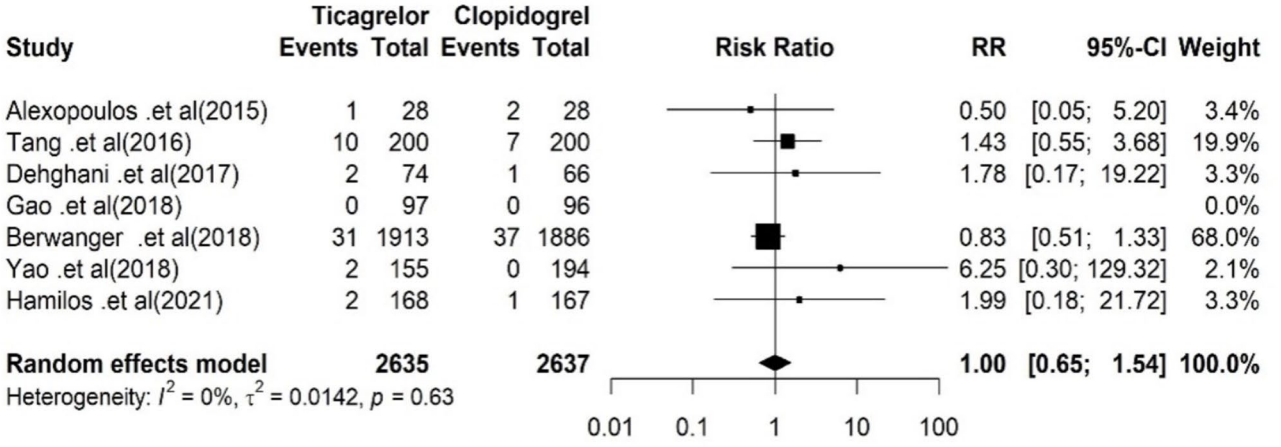


**Fig. 8** Overt bleeding in Ticagrelor and Clopidogrel groups

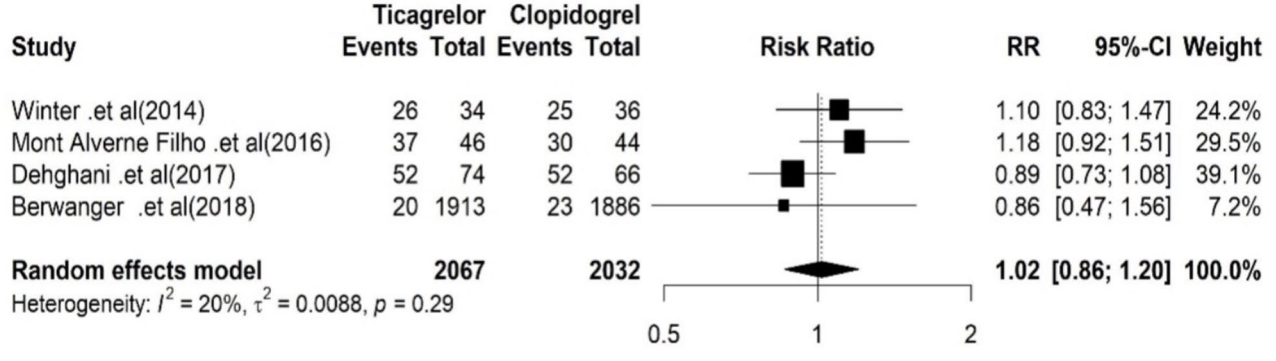


**Fig. 9** TIMI flow grade after Ticagrelor and Clopidogrel therapy

(p-value=0.043), while the publication bias was not statistically significant for the rest of the studied outcomes (p-value>0.05).

### Grading of recommendations assessment, development, and evaluation (GRADE) system results

GRADE [28] results for evaluating the strength of the obtained evidence are shown in Table 2. Based on the GRADE approach, the pooled RR value for the outcomes of Mortality, MACE, BARC, and TIMI Flow Grade was graded as High in terms of the strength of the evidence. On the other hand, the pooled RR value for the MI outcome was graded as Moderate because the publication bias in this outcome was uncertain.

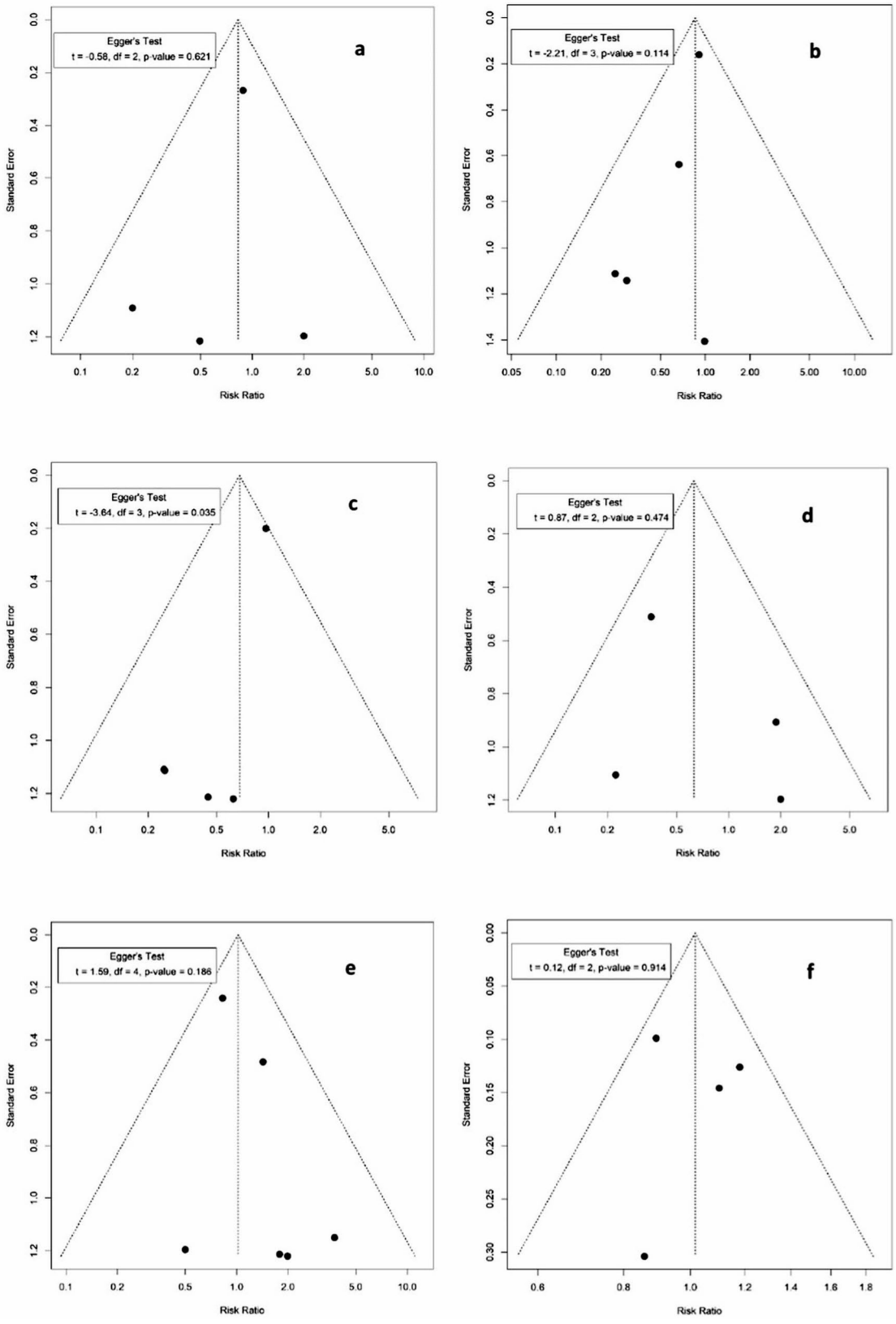


**Fig. 10** Funnel plots and Egger's regression test results for each outcome: **a** BARC, **b** MACE, **c** re-MI, **d** MORTALITY, **e** STROKE, **f** TIMI

**Table 2** Grade results

| Outcomes | Certainty assessment | | | | | | | № of patients | | Effect | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ticagrelor | Clopidogrel | Relative (95% CI) | |
| Mortality | 6 | RCT | Not serious | Not serious | Not serious | Not serious | None | 78/2480 (3.1%) | 91/2443 (3.7%) | **RR 0.857** (0.637 to 1.153) | ⨁⨁⨁⨁ High |
| MI | 6 | RCT | Not serious | Not serious | Not serious | Not serious | Publication bias is strongly suspected | 49/2467 (2.0%) | 58/2470 (2.3%) | **RR 0.680** (0.333 to 1.382) | ⨁⨁⨁◯ Moderate |
| Major Adverse Cardiovascular Events | 4 | RCT | Not serious | Not serious | Not serious | Not serious | None | 10/457 (2.2%) | 20/488 (4.1%) | **RR 0.630** (0.226 to 1.750) | ⨁⨁⨁⨁ High |
| BARC | 7 | RCT | Not serious | Not serious | Not serious | Not serious | None | 48/2635 (1.8%) | 48/2637 (1.8%) | **RR 1.020** (0.651 to 1.595) | ⨁⨁⨁⨁ High |
| TIMI Flow Grade Major | 5 | RCT | Not serious | Not serious | Not serious | Not serious | None | 135/2067 (6.5%) | 130/2032 (6.4%) | **RR 1.020** (0.860 to 1.201) | ⨁⨁⨁⨁ High |
| Stroke | 5 | RCT | Not serious | Not serious | Not serious | Not serious | none | 29/2312 (1.3%) | 36/2276 (1.6%) | **RR 0.830** (0.508–1.348) | ⨁⨁⨁⨁ High |

## Discussion

This systematic review and meta-analysis included 11 eligible studies with RCT design. The primary treatment strategy for 10,569 STEMI patients before and after either PPCI or fibrinolytic therapy was dual antiplatelet therapy with aspirin associated with Ticagrelor or Clopidogrel. Our study demonstrated that although the administration of Ticagrelor was associated with a decrease in mortality, stroke, recurrent MI, and MACE compared to receiving Clopidogrel, these findings were not statistically significant, which might be due to the small sample size. Furthermore, for the BARC score ≥ 3 and the TIMI flow grade, there were no significant differences between the two drugs in treating acute STEMI. Several systematic review and meta-analysis studies have recently investigated and compared the efficacy and safety of Ticagrelor and Clopidogrel drugs [21, 29, 30]. However, many of these studies have only included RCT studies conducted on ACS patients and have ignored the heterogeneity between primary studies. One of the important issues in the management of ACS patients is considering the type of ACS. Moreover, the treatment guidelines for STEMI and non-STEMI are entirely different. For example, STEMI patients should undergo PPCI as soon as possible, while the timing of PCI in non-STEMI patients has yet to be precisely known [31]. On the other hand, fibrinolytic therapy is prescribed in STEMI patients who cannot perform timely PPCI, while fibrinolytic drugs are not recommended in non-STEMI patients [20]. For this reason, in this systematic review and meta-analysis, we included only studies that included STEMI patients. In this way, the results of our research can provide more definitive evidence for the decision of doctors to choose between two anti-platelet drugs: Ticagrelor and Clopidogrel.

One of the most important issues that make a choice between Ticagrelor and Clopidogrel difficult is major bleeding. Since the balance between the benefits that the drug provides to the patient and the risk of causing side effects should be considered while choosing the drug, several studies and meta-analyses have investigated the impact of each of these drugs on the risk of major bleeding amongst ACS patients so far [32]. For instance, Fan et al. investigated the effect of these two drugs after PCI in ACS patients, and they found that the risk of major bleeding was higher in the Ticagrelor group [33]. Similarly, Guan et al. indicated that Ticagrelor was associated with a higher risk in this outcome [34]. In the meta-analysis conducted by Westman et al., although Ticagrelor was associated with a higher risk of bleeding, the difference was not significant. In our meta-analysis, there was no difference in the incidence of BARC score ≥ 3 between the two drugs in post-STEMI patients. The TIMI grade flow also has no significant differences in both groups.

Likewise, in the meta-analysis by Kheiri et al., which compared these two drugs in STEMI patients, none of the drugs was superior in creating a lower risk of major bleeding [35].

Ticagrelor has the potential to reduce the mortality rate, and the present study also showed a reduction in mortality rate due to the use of this drug compared to Clopidogrel. However, the result was not statistically significant. It must be taken into account that the risk of death in patients also highly depends on the type of ACS and the main treatment strategy [36]. Different clinical guidelines suggest the administration of P2Y12 receptor inhibitors along with aspirin for the management of both ACS and post-PCI patients. Also, many large RCTs have proven the superiority of Ticagrelor and Prasugrel over Clopidogrel. The European Society of Cardiology considers Ticagrelor and Prasugrel as better options than Clopidogrel regarding the rapid onset of action and greater potency [37].

One of the known complications that may occur after Acute Myocardial Infarction is ischemic stroke, which can have devastating consequences. One of the causes of ischemic stroke is the aggregation of platelets, and antiplatelet treatments interfere with this process; therefore, they have a preventive effect on stroke [38]. Clopidogrel and Aspirin are among the drugs approved by the US Food and Drug Administration for the secondary prevention of ischemic stroke [39]. In addition, the effectiveness of Ticagrelor for preventing ischemic stroke in patients with vascular risk factors has been shown in Dr. Malhotra et al. study; the researchers concluded that Ticagrelor could effectively reduce ischemic stroke in patients [40]. This finding was consistent with our study's results, which showed a decrease in the risk of stroke in patients who underwent treatment with Ticagrelor compared to those who received Clopidogrel. Although the results of our research were not statistically significant, this may be due to the small number of studies (5 studies) that reported this outcome. Also, many of the studies included in the present research excluded patients with a history of stroke.

Standard treatment guidelines recommend Dual Antiplatelet Therapy (DAPT) for ACS patients who should undergo PCI because this therapeutic combination reduces MACE [41]. Most patients are given dual antiplatelet therapy after PCI to reduce MACE due to the reocclusion of coronary arteries. Findings in the present study resulted in a decrease in the MACE in patients taking Ticagrelor comparing to those taking Clopidogrel, although this decrease was not statistically significant. Dr. Sun and his colleague's meta-analysis of comparing the clinical Outcomes Between ticagrelor and clopidogrel in ACS patients also did not prove the superiority of Ticagrelor over Clopidogrel in this outcome [42].

Notably, since there is a possibility of bleeding and upper gastrointestinal complications in patients who receive the combination of Clopidogrel and Aspirin, these patients are prescribed drugs, such as proton-pump inhibitors, which reduce the risk of bleeding by protecting the digestive tract mucosa, simultaneously [43]. However, the simultaneous use of two drugs, Clopidogrel and Pantoprazole, causes a disturbance in the mechanism of action of Clopidogrel, as a result of which the risk of MACE increases. Though Ticagrelor does not affect these mechanisms, it appears to reduce the incidence of MACE compared to Clopidogrel.

## Conclusions

According to the present study, the use of Ticagrelor in post-STEMI patients compared to Clopidogrel in combination with aspirin has shown a reduction in mortality, re-infarction, MACE, and ischemic stroke; however, these reductions were not statistically significant. In comparing the chance of major bleeding, there was no significant difference in the incidence of BARC score ≥ 3in using Ticagrelor compared to Clopidogrel has advantages such as higher TIMI flow grade and also showed no significant differences in the two groups. In line with the previous studies and meta-analysis, still, more studies are needed to be able to confirm the superiority of Ticagrelor over Clopidogrel in post-STEMI patients. which was consistent with the findings of the previous studies.

### Limitations

One of the issues that may lead to publication bias in this research is that we only included studies in English. The second limitation was that the Eager's test was not performed based on the existing guidelines because the number of studies for each outcome was below ten studies. Another concern is that the use of other drugs, including beta blockers, ACEI/angiotensin-renin blockers, and statins, might have affected the results. Moreover, comorbidities were excluded in the study, whereas obese patients and patients with diabetes should have been included. Additionally, Major trials were not included in this study.

#### Abbreviations

| | |
|---|---|
| STEMI | ST-segment elevation myocardial infarction |
| MACE | Major Adverse Cardiovascular Events |
| BARC | Bleeding Academic Research Consortium |
| TIMI | Thrombolysis in myocardial infarction |
| ACS | Acute Coronary Syndrome |
| NSTEMI | Non-ST-segment elevation myocardial infarction |
| MI | Myocardial infarction |
| IRA | Infarct-Related Artery |
| PPCI | Primary percutaneous coronary intervention |
| PI | Pharmacological Intervention |
| PCI | Percutaneous coronary intervention |
| RCT | Randomized Clinical Trial |
| HF | Heart failure |

GRADE Grading of Recommendations Assessment, Development, and Evaluation
DAPT Dual Antiplatelet Therapy

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**Author contributions**
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No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate**
Not applicable.

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**Competing interests**
The authors declare no competing interests.

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