Comparing Patient Profiles of Clopidogrel Versus Ticagrelor: A Systematic Literature Review and Meta-Analysis

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Introduction

- The ischemic benefit of ticagrelor over clopidogrel seen in randomized trial data has not been fully reproduced in real-world data.
- The discrepancies in efficacy or safety outcomes between the two therapies may be influenced by differences in prescribing practices for patients with ischemic and bleeding risk factors.
- We aimed to investigate if patients treated with clopidogrel are more likely to be at higher risk of ischemic and bleeding events than those treated with ticagrelor.

Objective

- To conduct a systematic literature review and meta-analysis to summarize the differences in patient profiles for clopidogrel versus ticagrelor in real world populations with ACS.

Methods

- A standardized review protocol was used to define eligibility criteria for the search and screening of references using the PICOs(TSS) framework, which outlines the population, interventions, comparators, outcomes, timing, setting, and study designs of interest (Table 1).
- MEDLINE (via PubMed) and Embase (via OVID) databases were searched for publications from inception to January 2018.
- Data extraction was conducted using the Digital Outcome Conversion (DOC) Data version 2.0 software platform (Doctor Evidence, LLC, Santa Monica, CA, USA) and its universal electronic extraction form, based on a standardized data configuration protocol. All characteristics were collected as reported in each paper and synonyms were bound before analysis using the DOG Ontology System.
- A pairwise meta-analysis was performed using a random-effects model to estimate odds ratios (OR) and mean differences (MD) with 95% confidence intervals (CI) to evaluate the magnitude and statistical significance of baseline characteristics between clopidogrel and ticagrelor groups.

Table 1. PICOs(TSS) criteria

| Population | Adult patients (age >18) with acute coronary syndrome (ACS), including STEMI, NSTEMI, UA |
| Interventions | Clopidogrel + Aspirin |
| Comparators | Ticagrelor + Aspirin |
| Outcomes | Baseline characteristics including: Patient demographics, Medical history, Management characteristics |
| Timing | No restriction to minimum treatment duration or follow-up, No restriction to outcome collected to certain time points |
| Setting/context | No restriction to study setting |
| Study design | Comparative observational studies |

Results

- The search identified 1,771 potential publications, of which 26 studies (190,662 patients) met eligibility criteria and were included in the analysis (Figure 1).

Figure 1. PRISMA flow diagram

- A total of 138,736 patients were treated with clopidogrel and 51,926 patients were treated with ticagrelor within the studies.
- Twenty-five key demographic, clinical and procedural variables were analyzed, and of these, 19 showed statistically significant differences between the treatment groups.
- Older age (MD 3.46; 2.54-4.38) and a higher percentage of females (OR 1.34; 1.26-1.43) was observed for clopidogrel compared to ticagrelor (Figure 2).
- Clopidogrel groups had higher percentages of bare metal stent placement (2.05; 1.56-2.68), multiple vessel disease (OR 1.20; 1.03-1.40), and prior percutaneous coronary intervention (PCI; OR 1.28; 1.09-1.51) or coronary artery bypass graft (CABG; OR 1.57; 1.23-2.00) compared to ticagrelor groups (Figure 2).

Figure 2. Patient demographics, procedural characteristics and revascularization history

- Clopidogrel groups also had significantly higher percentages of patients with prior CV events, such as prior stroke/transient ischemic attack (OR 1.59; 1.39-1.81) and prior myocardial infarction (OR 1.39; 1.16-1.65) (Figure 3).
- Significantly higher percentages of comorbidities were also observed for clopidogrel groups compared to ticagrelor, including hypertension (OR 1.23; 1.12-1.35), hyperlipidemia/dyslipidemia (OR 1.15; 1.04-1.26), peripheral artery disease (OR 1.60; 1.32-1.95), and diabetes (OR 1.24; 1.14-1.34) (Figure 3).
- In ticagrelor groups, greater percentages of drug eluting stent use, radial access, single vessel disease, and higher baseline BMI were observed.

Figure 3. Cardiovascular risk factors and comorbidities among clopidogrel-treated patients versus ticagrelor

Conclusions

- In comparison to patients treated with ticagrelor, clopidogrel-treated patients were more often older, female, treated using bare metal stents and had multiple vessel disease.
- In addition, a greater percentage of clopidogrel patients had previously undergone PCI or CABG, had previously had an MI, and had other comorbidities.
- These attributes may inform a higher ischemic/bleeding risk profile for patients treated with clopidogrel in comparison to ticagrelor.
- A higher prevalence of such medical history and comorbidities in clopidogrel-treated patients may indicate differences in prescribing practices, but further research is warranted.

Limitations

- This review and meta-analysis was conducted with observational studies rather than clinical trials, which is often considered a source of bias. For this topic, observational studies provide a more accurate assessment of prescribing behavior based on patient experience in the real world, however, there is an inherent bias.
- The analysis was performed using aggregate group data from published literature instead of individual patient data.

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