INPLASY PROTOCOL

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None declared.

Effectiveness and Safety of Single Antiplatelet Therapy with P2Y12 Inhibitor Monotherapy versus Dual Antiplatelet Therapy After Percutaneous Coronary Intervention for Acute Coronary Syndrome: A Systematic Review and Meta-Analysis

Chagas, GCL[1]; Chagas, RCL[2]; Rangel, AR[3].

Review question / Objective: **What are the effects of single antiplatelet therapy with P2Y12 inhibitor monotherapy versus dual antiplatelet therapy after percutaneous coronary intervention for acute coronary syndrome?**
Condition being studied: **Antiplatelet therapy after percutaneous coronary intervention for acute coronary syndrome.**
Information sources: **The databases will be Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica Database (Embase), and Cochrane Library. Searches were conducted on July 25, 2022 and will be updated on August 25, 2022. There will be no language or publication period restrictions.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 July 2022 and was last updated on 22 July 2022 (registration number INPLASY202270097).

INTRODUCTION

Review question / Objective: **What are the effects of single antiplatelet therapy with P2Y12 inhibitor monotherapy versus dual antiplatelet therapy after percutaneous coronary intervention for acute coronary syndrome?**

Condition being studied: **Antiplatelet therapy after percutaneous coronary intervention for acute coronary syndrome.**

METHODS

Participant or population: **We will include interventional studies comparing P2Y12 inhibitor monotherapy (e.g., clopidogrel,**

prasugrel, ticagrelor, ticlopidine) following a course of dual antiplatelet therapy (DAPT) with DAPT in adult (age ≥18 years) patients after percutaneous coronary intervention for acute coronary syndrome (ACS) with ≥3 months of follow-up, reporting the outcomes of interest. We will exclude ongoing studies, studies with overlapping patient populations, studies with no control group, studies with head-to-head comparisons of P2Y12 inhibitors, and studies that included patients with baseline indication for oral anticoagulant use (e.g., warfarin, dabigatran, and rivaroxaban).

Intervention: P2Y12 inhibitor monotherapy (e.g., clopidogrel, prasugrel, ticagrelor, ticlopidine) following a course of DAPT.

Comparator: DAPT.

Study designs to be included: Interventional studies (randomized controlled trials, case-control, and cohort [retrospective or prospective] studies).

Eligibility criteria: None.

Information sources: The databases will be Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica Database (Embase), and Cochrane Library. Searches were conducted on July 25, 2022 and will be updated on August 25, 2022. There will be no language or publication period restrictions.

Main outcome(s): Trial-defined major adverse cardiac event (MACE) and major bleeding event.

Additional outcome(s): Trial-defined major adverse cardiac and cerebrovascular events (MACCE), trial-defined net clinical adverse event (NACE), all-cause mortality, cardiovascular mortality, stent thrombosis, myocardial infarction, new-Q wave, revascularization, cerebrovascular event, any bleeding event, and clinically relevant nonmajor bleeding event.

Data management: The selection of studies will be carried out in three phases: reading of titles; reading of abstracts; and reading of full articles. The selection will be complemented by the search for experts in the field to find the most relevant studies on the subject. We will screen the reference lists of eligible studies to capture additional relevant citations. Literature selection and coding will be performed using Mendeley software version 1.19.8 (Elsevier, Amsterdam, NL).

The extracted data will be arranged in a spreadsheet in Microsoft Excel software version 2020 (Microsoft Corporation, Redmond, USA) and will consist of the following: study identification; publication year; country(ies) where study was performed; study design; time of follow-up; number of study participants; patients' age; interventions/exposures; comparator/control; primary endpoint; proportions of patients with ST-segment-elevation myocardial infarction (STEMI); proportions of patients with non- ST-segment-elevation myocardial infarction (NSTEMI); proportions of patients with hypertension; proportions of patients with diabetes; proportions of patients with dyslipidemia; proportions of patients currently smoking; proportions of patients with renal function impairment; proportions of patients with prior myocardial infarction; proportions of patients with prior cerebrovascular event; proportions of patients with prior PCI; proportions of patients with prior coronary artery bypass grafting surgery; number of lesions treated per patient; proportions of patients with lesion in the left main coronary artery; proportions of patients with lesion in the left anterior descending artery; proportions of patients with lesion in the left circumflex artery; proportions of patients with lesion in the right coronary artery; type of stent; rate of trial-defined MACE; rate of trial- defined MACCE; rate of trial-defined NACE; all-cause mortality; cardiovascular mortality; rate of stent thrombosis; rate of myocardial infarction; rate of new-Q wave; rate of revascularization; rate of cerebrovascular event; rate of any bleeding event; rate of clinically relevant nonmajor bleeding event, and rate of major bleeding event.

Study selection and data extraction will be performed by two review authors independently. Studies will be excluded if

there is inaccessibility of the full text. In the case of disagreement between the two reviewers, a third review author will be involved to resolve, by consensus, any discrepancies. In the case of duplicate studies and multiple reports from the same cohort, we will only examine (a) the largest cohort, (b) those with longer follow-up, or (c) the most recent one.
We will attempt to contact the original author by email correspondence to obtain any further information if not reported.

Quality assessment / Risk of bias analysis: We will assess the potential for bias of all studies selected for inclusion using the Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) tool for randomized trials and the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool for non-randomized studies. Two reviewers will independently assess the risk of bias in each study. In the case of disagreement between the two reviewers on the potential for bias assessment, a third review author will be involved to resolve, by consensus, any discrepancies. We will assess the strength of the body of evidence using The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Two reviewers will independently assess the strength of the body of evidence. In the case of disagreement between the two reviewers, a third review author will be involved to resolve, by consensus, any discrepancies.

Strategy of data synthesis: The systematic review and meta-analysis will be performed in line with recommendations from the Cochrane Handbook for Systematic Reviews of Interventions version 6.3, 2022, and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 statement guidelines. The meta-analysis will be performed using Review Manager (RevMan) [Computer program] software version 5.4 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2020). The data to be used will be the relative risk (RR) or the odds ratio (OR) with their corresponding 95% confidence intervals (CIs) for dichotomous outcome data, mean difference (MD) with its standard deviation (SD) for continuous outcome data, and hazard ratio (HR) with its corresponding 95% CI for time-to-event outcome data. We will assess the heterogeneity of included studies with the Chi2 ($\chi 2$, or chi-squared) test and the Thompson I2 index. We will consider P values of <0.10 as statistically significant when using the Chi2 test. We will regard I2 index values of <25%, 25% to <50%, 50% to <75%, and ≥75% as not important, moderate, substantial, and considerable heterogeneity, respectively. Heterogeneity will be explored by conducting subgroup analyses. The pooled weighted mean difference and 95% CIs will be estimated with a DerSimonian and Laird random-effects model. We will regard a P value of <0.05 as statistically significant. The evaluation of publication biases will be assessed using the funnel plot if there are at least ten studies included in the meta-analysis (k ≥10).

Subgroup analysis: We will attempt to perform subgroup analyses in the following subgroups:
- Randomized controlled trials.
- Randomized controlled trials and propensity score matched studies.
- Age (adults and elderly).
- Sex (male and female).
- Comorbidities (e.g., hypertension, diabetes).
- Type of ACS.
- Number of lesions treated per patient
- Potent P2Y12 inhibitors.
- Different P2Y12 inhibitors (e.g., clopidogrel, prasugrel, ticagrelor, ticlopidine).
- Doses of P2Y12 inhibitors.
- Duration of follow-up.
- Different definitions of major bleeding event.

Sensitivity analysis: We will perform sensitivity analyses for the main outcome(s) by excluding randomized trials that are judged to be at an overall "high" risk of bias and non-randomized studies that are judged to be at an overall "critical" or "serious" risk of bias.

Language restriction: None.

Country(ies) involved: Brazil.

Keywords: P2Y12 Inhibitor; Single Antiplatelet Therapy; SAPT; Dual Antiplatelet Therapy; DAPT; Percutaneous Coronary Intervention; PCI; Acute Coronary Syndrome; ACS.

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