Introduction: ST-elevation myocardial infarction (STEMI) is responsible for high morbidity and mortality, and new classes of drugs are being added to its treatment routine. The real benefit versus the bleeding risk of some associations is not yet known, given the large diversity of regimens and doses in the main clinical trials. It’s remains unclear if the bleeding risk of the increasing complexity of STEMI treatment, in terms of number of drugs - specially after the introduction of primary angioplasty (PA) - nullifies the clinical benefit.

Objectives: Assess, by systematic review and meta-analysis with indirect comparisons, the impact of the progressive addition of thrombolytics, anticoagulants, antiplatelets and primary PCI on 30-day outcomes: death, reinfarction (AMI) and major bleeding (MB) in patients with STEMI.

Methods:

**Medline search:** to identify studies in English and Spanish involving human adults with acute myocardial infarction with ST-segment elevation, randomized, comparing the classes of drugs: thrombolytics, antiplatelet agents and anticoagulants;


**Selection criteria:**

- **Population:** human adults;
- **Types of studies:** randomized / controlled (RCT);
- **Objective:** comparison of drugs in the treatment of STEMI.

- **Sample:** at least 500 patients.

- **Endpoints:** the trial should provide data on death, bleeding and infarction, reported in the period closest to 30 days.

**Statistic Analysis:**

- The arms of each study were grouped by similarity, according to the association of therapeutic classes*;
- Each class was considered used when, in the arm, at least 50% of patients had received it.
- Indirect comparisons between similar study arms was performed;
- A correlation between the number of classes utilized, the year and era of accomplishment and the adverse events cited was carried out based on the Spearman correlation coefficient;
- A binomial multivariate regression model was created, using the number of classes used and the execution of PA as independent variables, and the outcomes as response variables;
- The number of drugs: There was statistically significant Spearman correlation between the number drugs used in each group and the proportion of death (r = -0.466, p = 0.005) and bleeding (r = 0.403, p = 0.016) (Figures 2 and 3);
- No correlation was observed with reinfarction;
- The time correlation: The year of the study had a statistically significant correlation with the three outcomes: death (r = -0.380, <0.001), bleeding (r = 0.214, p = 0.013) and reinfarction (r = -0.231, p = 0.009);
- The five eras in which the study years were grouped (considering weight = 1 for every 5 years) had a statistically significant correlation with the outcomes: death (r = -0.325, p <0.001), bleeding (r = 0.214, p = 0.013) and reinfarction (r = -0.236, p = 0.007).

**Results:**

- The flowchart of article selection from PubMed search is in picture one;
- The studies included had a total of 403,556 patients, with overall average age of 61.0 years.
- **Risk factors:** hypertension: 39.9%; diabetes: 15.0%; smokers: 47.3%; previous AMI: 14.2%;
- The time-weighted average of events considered was 23.3 days.
- **Major bleeding criteria:** 19 different types of criteria for major bleeding were identified; the most used were TIMI criteria (21.1%), the need for any transfusion (18.8%) and GUSTO criteria (18.9%);
- **Number of drugs:** There were statistically significant Spearman correlation between the number drugs used in each group and the proportion of death (r = -0.466, p = 0.005) and bleeding (r = 0.403, p = 0.016) (Figures 2 and 3);

- **The multivariate regression model – random effects (Table 1):**
  - Negative correlation between the number of drugs used and mortality, and positive correlation between this number and the incidence of major bleeding (A).
  - PA also correlated with significantly reduced risk of death and increase in major bleeding (B).
  - In the presence of PA, the odds ratio for mortality reduction by the addition of a drug loses significance, indicating the additional benefit of intervention (C).

**Conclusion:** The increasing complexity of STEMI treatment (number of drugs) resulted in significant reduction in mortality and increased rates of MB, that does not nullify the net clinical benefit. AP seems to have additional benefit over each class added, along with increased bleeding risk. There is temporal trend towards reduction of mortality and increase of bleeding rates.