ANNEX 1
Data Source and Research

The following terms were used in our search: "acute myocardial infarction", "diabetes mellitus" and "stress hyperglycemia" and "stress hyperglycemia in acute myocardial infarction" and (ensaio clínico aleatório controlado OU ensaio clínico controlado OU randomizado OU placebo OU terapia medicamentosa OU aleatoriamente OU julgamento ou grupos NÃO animais) and (ensaio clínico randomizado controlado e humanos) and (ensaio clínico controlado aleatório e humanos).

During the search strategy, we selected the following languages: English, Spanish, and Portuguese. However, all relevant articles were published in English, conducted in human beings, and classified as RCTs.

– Definitions

Hyperglycemia in an acute myocardial infarction event was characterized according to the definition of each researcher. Usually, these definitions included the following terms from the MedDRA terminology: "hyperglycemia after acute myocardial infarction" and "hyperglycemia and mortality in acute myocardial infarction."

– Data Extraction and Quality Assessment

Two researchers who were not involved in any of the studies selected collected the data using a pre-set table and assessed, independently, the precision of the data, solving any discrepancies through consensus after a discussion with a third researcher. The following items were extracted from the studies included: name of the first author, year of publication, study design, characteristics of the patients, sample size, duration of the intervention, type of dose control, clinical outcomes, and adverse events. If a study was published more than once, we included the most recent report. If the patients were recruited for more than one study, they were not counted twice. The Cochrane Collaboration[1] tool to assess the risk of bias was used to assess the different types of bias within the studies included in our meta-analysis, and the quality of the study was assessed using the Grade[2] system. Two unblinded researchers independently assessed the potential risk of bias in the RCTs using the methods described in the Cochrane Collaboration guidelines. Our co-primary outcomes were: 1) Blood glucose levels after one of the approaches had been applied, and 2) mortality for each of the approaches.

– Studies Included and Excluded

Using the Medline/PubMed, Cochrane Library and ClinicalTrials.gov databases, we identified 36 citations that used the search terms previously defined. After implementing our inclusion/exclusion criteria, we excluded 25 studies that did not present data on mortality or a comparison between a more intensive approach for the control of stress hyper-

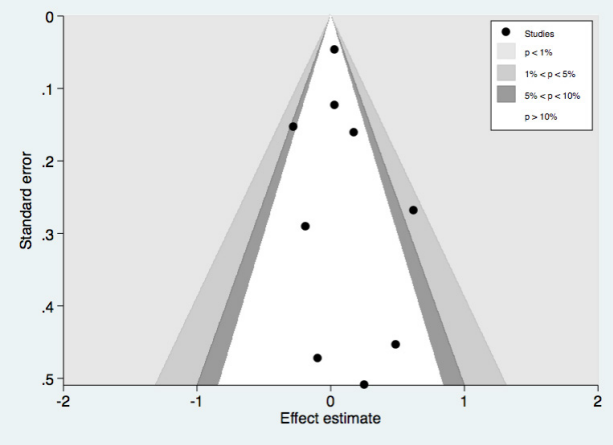

FIGURE 1

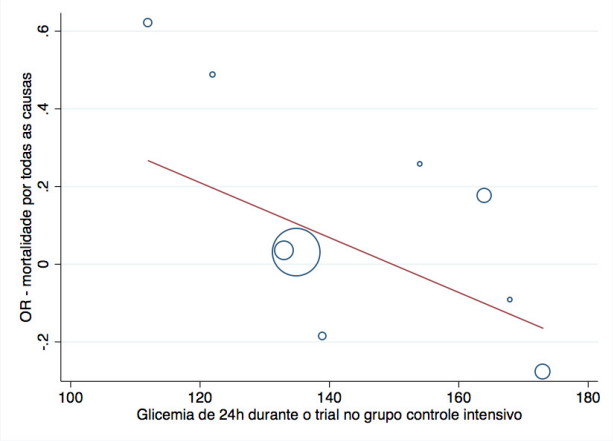

FIGURE 2

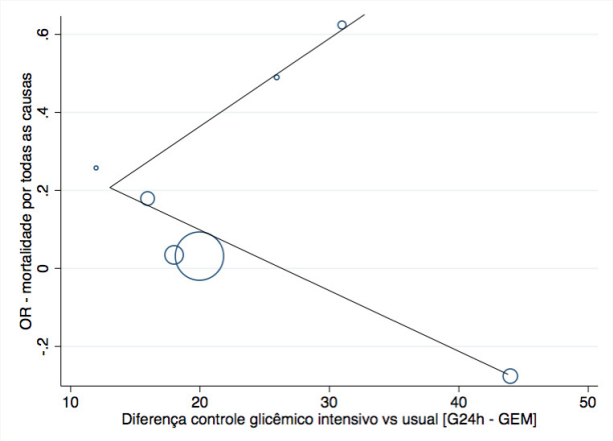

FIGURE 3

glycemia and more conservative approaches, or that presented randomization or data analysis (n=2) biases, or were previous meta-analysis, which then resulted in 11 studies considered relevant for this meta-analysis.

Data Handling and Analysis

Dichotomous variables are reported as percentages, while continuous variables are reported as average ± SD or median (interquartile range). The baseline data were obtained through weighted calculation. To identify the potential effects of the intensive strategy for blood glucose control, we calculated an overall risk ratio (RR) with meta-analyses of fixed and random effects models. Probability indexes and risk ratios were universally identical during the data analysis. We assessed the statistical heterogeneity between the trials using I^2 statistics (with 95% CI)[3], which provides a measure of the proportion of overall variation that can be attributed to heterogeneity between trials. We used risk ratios obtained through a fixed and random effects meta-analysis because they can be used as a sensitivity analysis. We used meta-regression analyses to investigate the possible sources of heterogeneity among the trials.

REFERENCES

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3. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-60.