Citation

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Review question

Does the use of anticoagulants affect patients with covid-19

Searches

We searched Cochrane COVID-19 register for randomised controlled trials and Observational study without any language restriction in PubMed, EMBASE, the Cochrane Library.

Types of study to be included

Randomised controlled studies (RCTs) and Observational study(OBs).

Condition or domain being studied

Effects of therapeutic and prophylactic doses of heparin on patients with COVID-19.

Participants/population

Patients with COVID-19 who will be included with mild, moderate and severe COVID-19 with any age.

Intervention(s), exposure(s)

Heparin?Heparinoids, Vitamin-K-antagonists, direct anticoagulants. All doses and regimens were eligible.

Comparator(s)/control

Standard of care, placebo or no intervention, other pharmacological and non-pharmacological interventions.

Main outcome(s)

Mortality.

Measures of effect

For continuous outcomes using the same scale we will perform analyses using the mean difference (MD) with 95% confidence intervals (CIs). For continuous outcomes measured with different scales, we will perform analyses using the standardised mean difference (SMD).

We will extract and report hazard ratios (HRs) for time-to-event outcomes.

For dichotomous outcomes, we will perform the analyses using the pooled risk ratio (RR) with a 95% CI.

Additional outcome(s)

- Length of stay in hospital

- Admission to the intensive care unit (ICU)

- minor adverse events and other advers events

- Serious adverse events

- Respiratory support

- Need for invasive mechanical ventilation

- Need for ECMO

- Hospital-acquired infection

Measures of effect

For continuous outcomes using the same scale we will perform analyses using the mean difference (MD) with 95% confidence intervals (CIs). For continuous outcomes measured with different scales, we will perform analyses using the standardised mean difference (SMD).

We will extract and report hazard ratios (HRs) for time-to-event outcomes.

For dichotomous outcomes, we will perform the analyses using the pooled risk ratio (RR) with a 95% CI.

Data extraction (selection and coding)

Two independent researchers will select and extract the data from the included studies. First, the articles will be selected based on the title and abstract. Second, full texts will be evaluated to include or exclude the studies; disagreements will be resolved by consensus and if it is necessary a third researcher will be included. Data regarding authorship, year of publication, patient description, interventions (intervention and control), absolute numbers of each outcome, and follow-up period will be extracted from the studies.

Risk of bias (quality) assessment

The risk of bias for RCT will be used from the Cochrane risk-of-bias (RoB 2) tool and other fundamental elements, being expressed as very serious, serious, or non-serious. The risk of bias assessment will be conducted by two independent reviewers, and in case of disagreement, a third reviewer will be deliberated on the assessment. The quality of the evidence will be extrapolated from the risk of bias and will be described by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) terminology as very low, low, or high.

We will use the RoB 2 Excel tool to implement RoB 2. The full RoB 2 data (e.g., completed Excel tool) will be stored in an online repository.

We will summarize the overall risk of bias for each result (outcome) according to RoB 2 guidance.

Strategy for data synthesis

Categorical outcomes will be expressed by group (intervention and control), the number of events, and calculated risk (in %) for each group (by dividing the number of events by the total number of patients in each group).We will use fixed-effect or random meta-analysis to evaluate the effect of anticoagulants vs. control on the outcomes when those data will be available in at least two RCTs. Effects of meta-analyses will be reported as risk differences (RD) and corresponding 95% CIs; a 95% CI including the number 0 in its range meant that there is no difference in the outcome effect between the intervention and control arms. The use of RD shows the absolute effect size in the meta-analysis when compared with a relative risk (RR) or odds ratio, and this technique can be used when the binary outcome is zero in both study arms. Heterogeneity of effects among studies will be quantified with the I^2 statistic (an $I^2 > 50\%$ means high heterogeneity). For the meta-analysis, we will use the Review Manager software, version 5.4 (RevMan 5; Cochrane Collaboration, Oxford, United Kingdom) or Stata software.

Analysis of subgroups or subsets

We will perform subgroup analyses to calculate RR, MD, or SMD in conjunction with the corresponding CI for each subgroup if statistical heterogeneity is present ($P < 0.01$ for the $?^2$ test of heterogeneity or a different clinical conclusion of 95% CI versus 95% PI).
We will perform subgroup analyses for the following characteristics:
-Subgroups will be considered according the COVID-19 severity

- Risk factors such as age, gender, comorbidities

- Severity of condition (moderate vs. severe disease as defined by the WHO clinical progression scale)

-Different dose of anticoagulants

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Type and method of review
Intervention, Meta-analysis, Systematic review

Anticipated or actual start date
30 November 2021

Anticipated completion date
01 February 2022

Funding sources/sponsors
National Natural Science Foundation of China State the funder, grant or award number and the date of award

Conflicts of interest

Language
English

Country
China

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Administration, Oral; Anticoagulants; Atrial Fibrillation; COVID-19; Humans; SARS-CoV-2

Date of registration in PROSPERO
24 November 2021

Date of first submission
24 November 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

24 November 2021