Study Protocol

ver.02
03/25/2020

Title:

Effect of remote ischemic preconditioning in improving postoperative pulmonary function in adult patients: A meta-analysis with trial sequential analysis

Registration information:

Pre-registration site: University Hospital Medical Information Network (UMIN)
Registration number: UMIN000030918

Purpose:

Effect of remote ischemic preconditioning on postoperative pulmonary function was controversial. The aim of this study is to investigate the effect of remote ischemic preconditioning on postoperative pulmonary function.

Methods:

This study is a systematic review and meta-analysis with trial sequential analysis.
We followed the recommendations of the PRISMA statement and Cochrane Handbook.

Search strategy

Databased searched

MEDLINE, CENTRAL, Embase, and Web of Science; the reference lists of the retrieved full articles are also searched. Further, we conduct a search of clinicaltrials.gov and the UMIN Clinical Trials Registry.

Date of search

We planned to search these databases at January 31, 2018.
We updated the search at December 2th, 2019.

The following search strategy combining free text and MeSH terms was set up for PubMed: This information is confidential.

Two authors independently scan the titles and abstracts of reports identified by the variety of search strategies described above. If eligibility cannot be determined from the title or abstract, the full paper is retrieved. Potentially relevant studies, chosen by at least one author, are retrieved and evaluated in full-text versions. The articles that meet the inclusion criteria are assessed separately by two authors, and any discrepancies are resolved through discussion.

Inclusion and Exclusion Criteria

We search for all randomized controlled trials that tested the effect of remote ischemic preconditioning on postoperative pulmonary function. We exclude data case reports, comments or letters to the editor, reviews, and animal studies. Eligibility is not restricted by language, type of surgery, anesthetic technique, or patient age.

Primary and secondary outcomes

The primary outcome of the present meta-analysis is the PaO2/FIO2 ratio 24 hours after surgery. The secondary outcomes are A-a DO2 and Respiratory index 24 hours after surgery, the length of mechanical ventilation, the incidence of complication, postoperative inflammation, the pH level 24 hours after surgery, and acute kidney injury.

Data Collection

A data collection sheet is created and included data on: (1) number of patients in study, (2) age, (3) sex, (4) ASA-Physical Status, (5) type of anesthesia, (6) type of surgery, (7) timing of remote ischemic preconditioning, (8) method of remote ischemic preconditioning, (9) the PaO2/FIO2 ratio after surgery, (10) the incidence of complication, (11) postoperative inflammation markers, (12) pH level, and (13) funding information. Values originally provided as percentages are converted back into actual numbers for analysis. If the data were reported only in graphs which indicated percentages or numbers of patients, we measure the lengths of the graphs to obtain the percentages or numbers of patients. Two authors extract the data independently from the studies included and then cross-check the data.

Assessment of risk of bias in individual studies

We assess the risk of bias as described by the Cochrane Handbook for Systematic Reviews of Interventions. We assess the risk of bias in sequence generation, allocation sequence concealment, blinding of patients, blinding of health care providers, blinding of data collectors, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other bias.

Assessment of quality of evidence

We grade the quality of evidence of the main outcomes using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach with GRADEpro software. Judgments of the quality of evidence are based on the presence or absence of the following variables: limitations in study design, inconsistency, indirectness, imprecision of the results, and publication bias. The quality of evidence for the main outcomes was graded as very low, low, moderate, or high.

Statistical Analysis

Continuous data are summarized using mean difference (MD) with a 95% confidence interval (CI). Dichotomous data are summarized using risk ratio (RR) with a 95% CI. If the 95% CI include a value of 0 or 1 for continuous or dichotomous data, respectively, we consider the difference not to be statistically significant. Heterogeneity is quantified with the I^2 statistic. We consider that significant heterogeneity existed when the I^2 statistic exceeded 50%. We plan to conduct subgroup analysis according to the following predefined factors when the I^2 statistic exceeded 50%: (1) type of anesthesia (inhaled vs total intravenous anesthesia), (2) type of surgery (lung resection or not), or (3) patients age (<18 years old or not). We use the random effect model (Dersimonian and Laird method) to combine the results. Forest plots are used to graphically represent and evaluate the effects of treatment. Small study effects is assessed using a funnel plot and an Egger's regression asymmetry test and is considered to be positive if $p < 0.1$ in the regression asymmetry test. Sensitivity analyses are performed for the primary outcomes according to the risk of bias (low vs. high or unclear). For our primary outcomes, trial sequential analysis (TSA) are performed to correct for random error and repetitive testing of accumulating and sparse data. TSA monitoring boundaries (i.e., monitoring boundaries for meta-analysis) and required information size (RIS) are quantified, and adjusted CIs are calculated. Risk of type 1 error is maintained at 5% with a power of 90%. The MD of the PaO2/FIO2 ratio 24 hours after surgery of 50 was

considered clinically meaningful. If the TSA-adjusted CI included a value of 0, we consider the difference not statistically significant.

Software used for statistical analysis

Statistical analyses are performed using the R statistical software package, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria). TSA is performed using TSA viewer version 0.9.5.10 β (www.ctu.dk/tsa).

Study Protocol

ver.01
01/21/2018

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Primary and secondary outcomes

The primary outcome of the present meta-analysis is the PaO2/FIO2 ratio 24 hours after surgery. The secondary outcomes are the incidence of pulmonary complication, postoperative inflammation, acute kidney injury, cardiac function.

Data Collection

A data collection sheet is created and included data on: (1) number of patients in study, (2) age, (3) sex, (4) ASA-Physical Status, (5) type of anesthesia, (6) type of surgery, (7) timing of remote ischemic preconditioning, (8) method of remote ischemic preconditioning, (9) the PaO2/FIO2 ratio after surgery, (10) pulmonary complication, (11) postoperative inflammation markers, (12) incidence of acute kidney injury, (13) cardiac function, (14) pH level, and (15) funding information. Values originally provided as percentages are converted back into actual numbers for analysis. If the data were reported only in graphs which indicated percentages or numbers of patients, we measure the lengths of the graphs to obtain the percentages or numbers of patients. Two authors extract the data independently from the studies included and then cross-check the data.

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