

Research Design and Data Analysis

Official Title of the study: Establishment of Systemic Prevention and Management for Perioperative Hypothermia and Its Effect on Patients Outcome—a Prospective Multiple Centers Randomized Controlled Study

Identifiers: [NCT ID not yet assigned]

Unique Protocol ID: *Hypothermia2018*

Brief Title: Systemic Prevention and Management for Perioperative Hypothermia and Its Effect on Patients Outcome

Latest edition: September 20th 2018

Research Designing

Specific aim

To determine the efficacy of different warming method according to hypothermia risk estimation to prevent perioperative hypothermia and reduce perioperative complications.

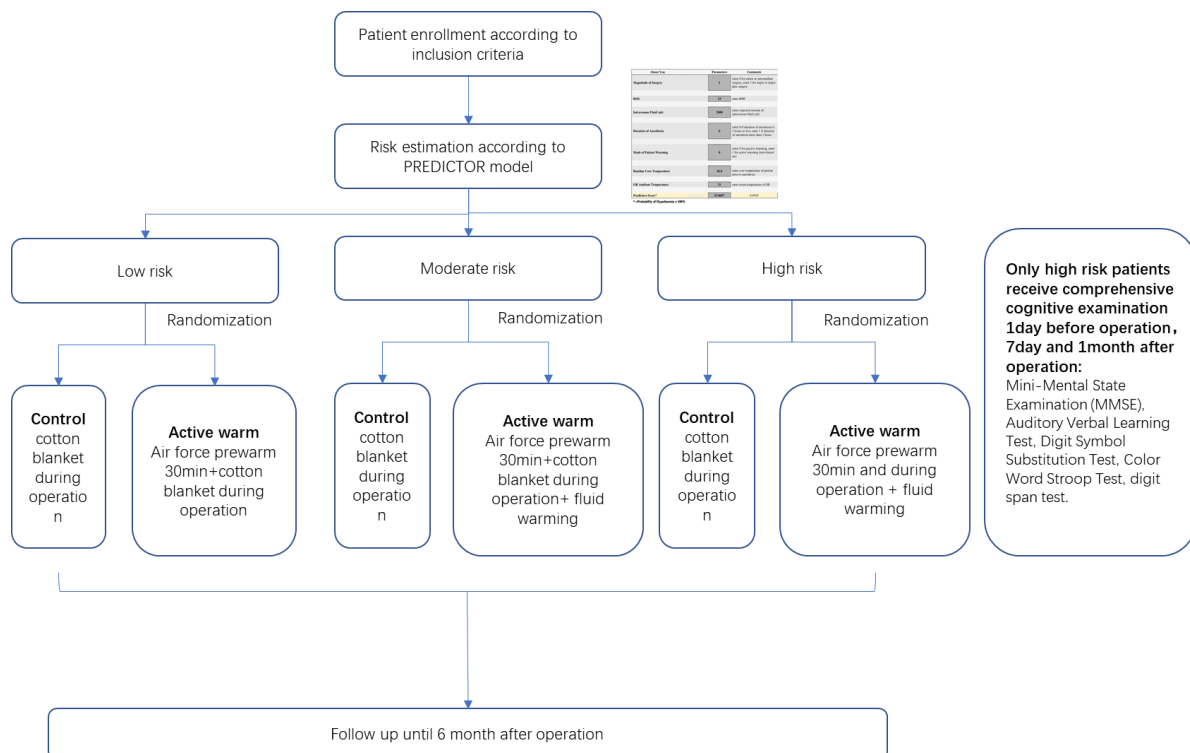
Methods

Overview of design

This is a randomized, single-blinded, multi-center study clinical trial to determine both clinical outcomes of stratified warm strategy to prevent intraoperative hypothermia. Patients enrolled into this trial will be from elective major surgery population in PUMC Hospital, Beijing Hospital and Xuanwu Hospital from April 1, 2019 to March 31, 2021. We plan to enroll approximately 800 patients. We review the medical records and have a face-to-face interview to determine whether the patient is eligible for the study according to the inclusion and exclusion criteria. Hypothermia risk will be estimated through PREDICTOR model^[1] in all eligible patients. According to hypothermia risk level, these patients will be stratified into high, moderate and low risk group. Patients in each group will be randomly categorized into warm group and control group. For control group traditional passive warm was used, which means cotton blanket was used to prevent hypothermia. While, for active warm group, different warm strategy are used according to risk level, prewarm for 30min only for low risk patients, prewarm 30 min and fluid warm for moderate risk patients, prewarm and forced-air warm throughout operation and fluid warm for high risk patients. Temperature will be record though the operation. All participants were followed up every day after surgery until 6 month after operations. Any post operation complication will be recorded carefully.

Measurements

Intervention: traditional cotton blanket warm vs. active warm according to risk level



Plans for randomization and blinding

Randomization: Patients will be randomized using stratified blocked randomization. The random treatment assignments are placed in sealed, numbered, and opaque envelopes who will not be involved in opening them. Two staffs signed and recorded the next unopened envelope before opening the envelope. Investigators will access the allocation about an hour before surgery is expected to start, after consent is obtained. Allocation will thus be remained concealed until the last practical moment.

Blinding: Patients are all blind to the allocation.

Reduce confounding factor: Patients in GA group were given 1.5-2mg/kg Propofol, 0.8mg/kg rocuronium, 2ug/kg fentanyl for induction of anesthesia. After tracheal intubation, anesthesia was continued with sevoflurane in 50% nitrous oxide with oxygen, and end-tidal anesthesia gas is maintained 0.9-1.2 MAC. Supplemental fentanyl doses of 50ug are administered for blood pressure elevation or heart rate increases amounting to more than 10% of baseline.

Outcome variables

Primary outcome: hypothermia incidence during operation

Secondary outcome:

2. The amount of Intraoperative blood loss/blood transfusion

[Time Frame: During operation]

3. Length of stay in PACU

[Time Frame: Postoperative during in postanesthesia care unit, up to 24 hours after surgery]

4. The incidence of Surgical site infection

[Time Frame: Within 30 days postoperative]

5. Length of Stay in hospital

[Time Frame: inpatient period, up to 6 month after surgery]

6. Length of Stay in ICU

[Time Frame: inpatient period, up to 6 month after surgery]

7. Incidence of Adverse cardiovascular events

[Time Frame: Within 6 month post operation]

8. Incidence of shiver

[Time Frame: during in postanesthesia care unit, up to 24 hours after surgery]

9. Mini-Mental State Examination (MMSE),

It's a score to evaluate cognitive function. Total score is 30. Higher values represent a better cognitive function.

[Time Frame: One day preoperation and 1, 7, 30 days postoperation]

10. digit symbol substitution test

The digit symbol substitution test is an evaluation tool used to assess cognitive functioning. It initially was part of the Wechsler Adult Intelligence Test (WAIS), a well-known test that measures an individual's attention. Lower digit symbol test scores were correlated with a higher risk of developing dementia in both the five and 10 year groups. Higher values represent a better cognitive function.

[Time Frame: One day preoperation and 1, 7, 30 days postoperation]

11. Auditory Verbal Learning Test,

a memory test that involves learning verbal material, usually single words presented in a list, that is continually presented over repeated trials. Higher values represent a better memory functions.

[Time Frame: One day preoperation and 1 , 7, 30 days postoperation]

12. Color Word Stroop Test

The Stroop Colour and Word Test (SCWT) is a neuropsychological test extensively used to assess the ability to inhibit cognitive interference that occurs when the processing of a specific stimulus feature impedes the simultaneous processing of a second stimulus attribute, well-known as the Stroop Effect. Higher values represent a better ability to inhibit cognitive interference.

[Time Frame: One day preoperation and 1 , 7, 30 days postoperation]

13. digit span test.

a memory test that involves remember a series of numbers test short time memory Higher values represent a better memory functions.

[Time Frame: One day preoperation and 1 , 7, 30 days postoperation]

14. postoperative cognitive dysfunction incidence

- $Z \text{ score} = (\text{postoperative score} - \text{preoperative core}) / \text{SD of non-surgical group}$
- Two or more than two item in cognitive examination $Z \text{ score} < -1.96$
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[Time Frame: One day preoperation and 1 , 7, 30 days postoperation]

Statistical issues

Analysis plan

Student's t test (for Intraoperative blood loss/blood transfusion, Length of stay in PACU)
Wilcoxon rank-sum test (for Length of Stay in hospital, Length of Stay in ICU, MMSE, AVLT, Digital span, Color Word stroop , digit symbol substitution),
 χ^2 test (for hypothermia incidence, Incidence of shiver, Surgical site infection: Within 30 days postoperative, Adverse cardiovascular events: Within 30 days postoperative, Incidence of postoperative cognitive disorder at 7 day postoperative) will be used to compare the primary and secondary outcomes between groups.

Sample size estimates

α (two-sided) = 0.05, power $(1 - \beta) = 0.90$ A previous study revealed that hypothermia incidence is 39.9% [2]. The control and warming group is 1:1. According to our preresearch Warming effect size = 0.36, 10% drop-out, 793 patients are required in total.

Data safety and monitoring

Because the study is a small trial with interventions likely to be safe, an experienced anesthesiologist and an orthopedist who are not involved in the study will monitor the safety and the trial procedures. They meet at the trial design period, prior to start of recruitment (review the study protocol), and every 3 months after start of the recruitment.

The members of the DSMB should review recruitment, randomization, adherence to blinding, potential complications of epidural puncture, data accuracy and integrity.

References

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[2] Yi J, Lei Y, Xu S, Si Y, Li S, Xia Z, Shi Y, Gu X, Yu J, Xu G, Gu E, Yu Y, Chen Y, Jia H, Wang Y, Wang X, Chai X, Jin X, Chen J, Xu M, Xiong J, Wang G, Lu K, Yu W, Lei W, Qin Z, Xiang J, Li L, Xiang Z, Pan S, Zhan L, Qiu K, Yao M, Huang Y. Intraoperative hypothermia and its clinical outcomes in patients undergoing general anesthesia: National study in China. *PLoS One.* 2017 Jun 8;12(6):e0177221. doi: 10.1371/journal.pone.0177221. eCollection 2017. PubMed ID: 28594825

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