Impact of Inhalational versus Intravenous Anaesthesia on Early Delirium and Long-term Survival in Elderly Patients after Cancer Surgery: a Multicenter, Open-label, and Randomized Controlled Trial

Description of the trial and written informed consent

We invite you to participate in this multicenter, open-label, randomized controlled trial investigating the "Impact of Inhalational versus Intravenous Anaesthesia on Early Delirium and Long-term Survival in Elderly Patients after Cancer Surgery". Before you decide to participate in the study, please read the following description carefully which will help you to understand the purposes and contents of the study and to know the potential benefits from the study that it may bring to you, as well as the potential risks that you may encounter during the study. You are welcome to discuss your concerns with your doctors, relatives and/or friends as you wish before making the decision. If you have any questions or would like to get more information about the study, please do contact us. If you are participated in another study, please inform your research doctor.

The study is organized by Peking University First Hospital (principal investigator [PI]: Professor Dong-Xin Wang), and will be performed in 17 tertiary hospitals, including Peking University Hospital of Stomatology (PI: Professor Xu-Dong Yang), Fourth Hospital of Hebei Medical University (PI: Professor Hui-Qun Jia), Ningxia People's Hospital (PI: Professor Qing-Shan Ye), Beijing Cancer Hospital (PI: Professor Hong-Yu Tan), Beijing Shijitan Hospital (PI: Professor Bin-Jiang Zhao), Guizhou Provincial People's Hospital (PI: Professor Fang-Xiang Zhang), Qinghai University Affiliated Hospital (PI: Professor Zhen Jia), The Third Xiangya Hospital of Central South University (PI: Professor Wen Ouyang), Affiliated Tumor Hospital of Guangxi Medical University (PI: Professor Ling-Hui Pan), Shanxi Provincial People's Hospital (PI: Professor Yong-Qing Guo), Zhongda Hospital Southeast University (PI: Professor Ning Yin), the First Affiliated Hospital of Zhengzhou University (PI: Professor Yan-Qu Ai), Tang-Du Hospital Fourth Military Medical University (PI: Professor Xu-De Sun), Shanxi Provincial Cancer Hospital (PI: Professor Qin-Gong Zhang), Tianjin Nankai Hospital (PI: Professor Jian-Bo Yu), and Shenzhen Second People’s Hospital (PI: Professor Zhi-Heng Liu).

1. What are the purposes of this study?
Delirium commonly occurs in the elderly after surgery. It can present as inability to concentrate, perception disturbances, changes in your level of consciousness and normal thinking impairment. Patients who develop delirium after surgery have long hospital stay, decreased quality of life and increased mortality. We don't know exactly why or how delirium occurs, but we do know that it is closely related to old age, major surgery and postoperative pain. As a current routine practice, elderly patients undergo major surgery under either inhalational anaesthesia or intravenous anaesthesia. The purpose of this study was to compare the impact of inhalational versus intravenous anaesthesia on early delirium and long-term survival after cancer surgery.

2. Who are invited to participate in this study?
Patients with age ≥ 65 years, who are diagnosed as primary cancer, do not receive radio- or chemotherapy before surgery, do not have critical illness or history of mental illness, and are scheduled to undergo surgery for cancer under general anesthesia will be invited.

3. How many patients are participating in this study?
We plan to enroll 1200 participants among patients in the above 17 hospitals; of those, 600 patients will be enrolled in Peking University First Hospital.

4. How does the study look like?
Patients in this study will be randomized into two groups. In the Group A, they will receive inhalational (sevoflurane) anaesthesia; whereas patients in the Group B will receive intravenous anaesthesia. These two anaesthesia techniques are routinely used in daily practice. Since it is a randomized trial, each participant will have the same possibility (i.e., 50%) to be enrolled in either the group A or B, just as throwing coins, which is not subjected to any individual’s personal choice.

5. If I participate, what do I need to do?
If you agree to participate in this study, we will give a recruitment number and establish medical records for you. We will collect your demographic and baseline medical data and assess your cognitive function and delirium status before surgery. We will assess your pain severity and delirium occurrence twice daily during postoperative days 1 to 7. Each assessment will last about 5 minutes. After which, we will see you weekly and record the occurrence of other complications. At 30 days after surgery, we will see you and call you (in case you have been discharged from the hospital) to assess your health status and ask you to do a cognitive function test. You will be followed up (by telephone) once a year for 3 years after surgery by the investigators. At the end of the 3rd year after surgery, we will assess the quality of life (assessed with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC QLQ-C30) and cognitive function (assessed with the Telephone Interview for Cognitive Status-Modified) through telephone. All the above interviews and assessments are free of charge. The only thing you need to do is to cooperate with our investigators wherever you can.

6. Are there any potential risks or harmful effects on me?
In the present study, the intervention measures are two anaesthetic techniques currently being used during daily practice. Therefore, our study will not produce any additional risks on participants. However, adverse events may occur even during daily anaesthesia. In such case, anesthesiologists will manage these events according to routine practice. Anaesthesia related adverse events may include but not limited to the following: drug allergy, allergic shock; adverse events related to fluid infusion or blood transfusion; congestive heart failure, arrhythmia, myocardial ischemia, myocardial infarction, pulmonary embolism, cardiac arrest; aspiration induced asphyxia, aspiration pneumonia, atelectasis, pulmonary edema, respiratory failure; cerebral vascular accident, aggravated neuropsychiatric disease; hepatic or kidney insufficiency; invasive monitoring related infection, hematoma, pneumothorax, hemothorax and etc.
Endotracheal intubation related adverse events may include but not limited to the following: teeth injuries, tracheotomy for difficult airway, laryngospasm, bronchospasm, laryngeal edema, delayed anaesthesia emergence and etc.

Postoperative analgesia related adverse events may include but not limited to the following: nausea, vomiting, dizziness, hypotension, pruritus, inadequate analgesia, urinary retention and etc.

The anaesthesiologists will perform anaesthesia and perioperative care according to your individual conditions in order to minimize the potential risks. In case of any adverse events, the anaesthesiologists will manage promptly in order to ensure your safety. If you feel any discomforts, your conditions have any changes or you meet any unexpected events, please promptly inform your doctors and he or she will make judgments and provide proper managements. Anaesthesiologists and other care providers/doctors will act to ensure your safety. In case of a severe adverse event, except active and prompt treatment, the principal investigator and the Ethics Committee will be reported and further treatments and/or care will be in place if necessary.

Of note, it is true that any medical treatments may produce adverse events, but we will put your safety as our priority. In addition, if anesthesiologists find that the anaesthesia method is ineffective, they will stop the study and change to other effective anaesthesia methods. However, available evidences suggest that both anaesthesia methods used in this study are relative safe and effective.

7. Do I get any benefit from participating in the study?
Participation in the study will help us to diagnose and treat delirium earlier. The results of this study may help to improve the postoperative management of patients in the future and bring benefits to more patients.

8. Are there any alternative treatments, if I do not participate in this study?
You may choose not to participate in this study. This will not affect any treatments that you should receive. Anaesthesiologists will perform either inhalational or intravenous or combined (that means both inhalational and intravenous anesthetics are used) anaesthesia for you during surgery.

9. Do I have to attend and complete this study?
The decision to participate in the study is entirely voluntary. It is your right to make the decision whether you participate or not and you can withdraw consent at any time without giving any reasons during the study. If you decide to participate, please sign the written informed consent form. Withdrawal from the study does not affect your treatments throughout your hospital stay. In such case, your data and information will not be used in the study. On the other hand, if you or we think the study is affecting your normal treatment or outcome, the researchers will also stop the study. During the period of study participation, please tell researchers your true medical history and current physical status, as well as whether you have participated in any other studies undergoing currently or recently, or if you have any newly developed discomfort. If you do not abide the study protocol or develop any study-related harmful effect, the researchers can terminate your participation in the
study.

If the study is terminated prematurely, we will keep you informed immediately and your doctor will give you advice on your further treatment. If you withdraw from the study, we have the plan of last follow-up for your own safety purpose; but you have the right to refuse. We may also contact you if we find any new information about your health or your rights.

10. Will participation in this study bring me extra cost?
Participation in the study will not bring you extra cost. The follow-ups and assessments of delirium, pain, cognitive function and beyond are all free; but normal medical expenses including medications, use of equipments, examinations, surgeries, and nursing care during your hospitalization are at your expense.

11. Will participation in this study bring me reward?
Participation in the study will not gain any extra rewards.

12. What is about the handling of related injury?
The anaesthesia methods adopted during the study are routinely used in daily practice. Participation in the study does not bring you any additional risk. If your health is compromised during anaesthesia and surgery, the hospital will provide necessary medical care promptly and manage the problem accordingly.

13. Will my personal information be confidential?
If you decide to participate, your participation in the study and your personal data during the study are confidential. Non-research team members will not be allowed to obtain your information, unless permitted by PI. All research team members and institutions involved in the study will maintain confidentiality of your information (recorded in written or other formats). Your research information will be preserved for 5 years and then will be destroyed at the end of 5th year after the study. If the research information needs to be preserved for more than 5 years, we will obtain your permission via telephone, and will inform you how long and in what way your information will be preserved and used in the future. However, research information that is recorded in your medical record will be permanently retained. Some data obtained from you during the study will be published in the form of scientific papers, but your personal information (including name, age, education, etc.) will be kept confidential and your personal privacy will be protected according to law. In order to ensure that the study is carried out in accordance with the regulations, administrative members or the Ethics Committee members may access your personal information when necessary.

14. How can I get more information?
If you have any questions about the study, or suffer from any discomfort or injury during the study, or would like to obtain more information of the study, please do not hesitate to contact the research members: Dr. ****. Tel: ********.

If you have any questions regarding the ethical issues of the study, or would like to report any difficulty, dissatisfaction or worries during the study, or would like to provide suggestions for the study, please contact the Clinical Research Ethics Committee of *****
Hospital. Tel: ********.

Wherever necessary, you may also wish to contact the Department of Medical Service of ****Hospital. Tel: ********.
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Signature page

Statement of researcher:
I have explained the background, purposes, process, risks and benefits of the study entitled "Impact of Inhalational versus Intravenous Anaesthesia on Early Delirium and Long-term Survival in Elderly Patients after Cancer Surgery" to the participant, have allowed enough time for him/her to read the informed consent and to discuss with others, and have answered questions concerning the study. I have informed the participant to contact doctors *** (Tel: ******* or *** (Tel: ******* if he/she has any questions about the study, or contact the Department of Medical Service (Tel: ******* or the Clinical Research Ethics Committee (Tel: ******* if he/she has any questions regarding the ethical issues of the study. I have told the participant that he/she can withdraw consent at anytime during the study and that he/she will receive a copy of this informed consent form with signatures of both parties.

Signature of researcher: Date:

Statement of participant or participant’s legally acceptable representative:
I am well informed about the study protocol and understand the background, purposes, process, risks and benefits of the study. I have enough time and opportunity to ask questions, and I have been answered with satisfaction. I am also informed whom I should contact when I have questions, difficulties, worries, or suggestions, or want to obtain more information about the study.

I have read the informed consent of this study carefully and would like to participate in the study. I will cooperate with the research members according to the study protocol and the contents listed in informed consent, and will participate in the trial throughout the entire course of the study. I know that I can withdraw from the study at any time during the study without giving any reasons. I am informed that I will receive a copy of this informed consent form that is signed by the both parties.

Signature of participant: Date:

Tel: Address:

(In case the participant is unable to provide informed consent)

Signature of legally authorized representative: Date:

Relationship between legally authorized representative and participant:
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Written informed consent v3.5 (20170419)