INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Effects of propofol-based total intravenous anesthesia versus inhalation anesthesia on long-term survival in patients undergoing cancer surgery: a systematic review and meta-analysis

Tang, YX[1]; Tang, LL[2]; Yao, YT[3]; Huang, H[4]; Chen, B[5].

Review question / Objective: **To compare the effects of propofol-based total intravenous anesthesia with inhalation anesthesia on long-term survival of cancer surgery. (1) Patients: all patients undergoing cancer surgery with intravenous or inhalation anesthesia. (2) Intervention: propofol-based total intravenous anesthesia. (3) Comparator: inhalation anesthesia. (4) Outcomes: overall survival, recurrence- free or disease-free survival. (5) Study design: randomized-controlled trials and observational studies (prospective or retrospective).**
Information sources: **We will systematically search the following electronic databases (PubMed, Medline, Embase, and the Cochrane Library) from inception to July 2022 for eligible studies. Any potentially relevant studies will be manually searched based on the references of the identified studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 July 2022 and was last updated on 06 July 2022 (registration number INPLASY202270025).

INTRODUCTION

Review question / Objective: **To compare the effects of propofol-based total intravenous anesthesia with inhalation anesthesia on long-term survival of cancer surgery. (1) Patients: all patients undergoing cancer surgery with intravenous or inhalation anesthesia. (2) Intervention: propofol-based total intravenous anesthesia. (3) Comparator: inhalation anesthesia. (4) Outcomes: overall**

survival, recurrence- free or disease-free survival. (5) Study design: randomized-controlled trials and observational studies (prospective or retrospective).

Condition being studied: Cancer recurrence and metastasis after surgery account for a significant reason for cancer-related mortality. Our immune system constitutes the most predominant line of defense against cancer invasion. Emerging evidence has demonstrated that various anesthetic agents may influence the immune system during the perioperative period. Propofol has been suggested to have immunoprotective effects, while inhalation anesthetics may impair immunity. Whether different anesthetic regimes influence the long-term survival of cancer patients remains unresolved. Though several retrospective cohort studies have been published to address the effects of propofol-based total intravenous and inhalation anesthesia on long-term oncological outcomes, the conclusions remain conflicting. The optimal anesthetic choice for cancer patients in clinical practice needs to be further explored.

METHODS

Search strategy:

Pubmed

#1 MeSH descriptor: [Anesthesia, Intravenous] explode all trees #2 MeSH descriptor: [Anesthesia, Inhalation] explode all trees #3 MeSH descriptor: [Anesthetics, Inhalation] explode all trees #4 MeSH descriptor: [Anesthetics, Intravenous] explode all trees #5 anesthesia [TIAB] OR anaesthesia [TIAB] OR anesthetic [TIAB] OR anesthetics [TIAB] OR anaesthetic [TIAB] OR anaesthetics [TIAB] #6 intravenous [TIAB] OR inhalation [TIAB] OR inhalational [TIAB] OR volatile [TIAB]

#7 #5 AND #6

#8 TIVA [TIAB] OR propofol [TIAB] OR sevoflurane [TIAB] OR enflurane [TIAB] OR isoflurane [TIAB] OR desflurane [TIAB] OR halothane [TIAB]

#9 #1 OR #2 OR #3 OR #4 OR #7 OR #8

#10 MeSH descriptor: [Neoplasms] explode all tree #11 neoplasia [TIAB] OR neoplasias [TIAB] OR neoplasm [TIAB] OR neoplasms [TIAB] OR tumor [TIAB] OR tumors [TIAB] OR tumour [TIAB] OR tumours [TIAB] OR cancer [TIAB] OR cancers [TIAB] OR malignancy [TIAB] OR malignancies [TIAB]

#12 #10 OR #11

#13 MeSH descriptor: [Mortality] explode all tree #14 MeSH descriptor: [Survival Rate] explode all trees #15 MeSH descriptor: [Survival Analysis] explode all trees #16 MeSH descriptor: [Kaplan-Meier Estimate] explode all trees #17 MeSH descriptor: [Proportional Hazards Models] explode all trees #18 MeSH descriptor: [Neoplasm Recurrence, Local] explode all trees #19 MeSH descriptor: [Recurrence] explode all trees #20 mortality [TIAB] OR survival [TIAB] OR "Kaplan-Meier" [TIAB] OR "proportional hazard model" [TIAB] OR "cox regression" [TIAB] OR "recurrence-free survival" [TIAB] OR "disease-free survival" [TIAB] OR recurrence [TIAB]

#21 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20

#22 #9 AND #12 AND #21

Medline

#1 TS=(Anesthetics, Inhalation) OR TS=(Anesthetics, Intravenous) OR TS=(Anesthesia, Intravenous) OR TS=(Anesthesia, Inhalation) #2 TS=(anesthesia) OR TS=(anaesthesia) OR TS=(anesthetic) OR TS=(anesthetics) OR TS=(anaesthetic) OR TS=(anaesthetics) #3 TS=(intravenous) OR TS=(inhalation) OR TS=(inhalational) OR TS=(volatile)

#4 #2 AND #3

#5 TS=(TIVA) OR TS=(propofol) OR TS=(sevoflurane) OR TS=(enflurane) OR TS=(isoflurane) OR TS=(desflurane) OR TS=(halothane)

#6 #1 OR #4 OR #5

#7 TS=(neoplasia) OR TS=(neoplasias) OR TS=(neoplasm) OR TS=(neoplasms) OR TS=(tumor) OR TS=(tumors) OR TS=(tumour) OR TS=(tumours) OR TS=(cancer) OR TS=(cancers) OR TS=(malignancy) OR TS=(malignancies)

#8 TS=(mortality) OR TS=(survival) OR TS=("Kaplan-Meier") OR TS=("proportional hazard model") OR TS=("cox regression") OR TS=("recurrence-free survival") OR TS=("disease-free survival") OR TS=(recurrence)

#9 #6 AND #7 AND #8

Embase and Cochrane Library

#1 intravenous anesthesia [emtree term-exploded] OR inhalation anesthesia [emtree term-exploded] #2 anesthesia [ti,ab,kw] OR anaesthesia [ti,ab,kw] OR anesthetic [ti,ab,kw] OR anesthetics [ti,ab,kw] OR anaesthetic [ti,ab,kw] OR anaesthetics [ti,ab,kw]
#3 intravenous [ti,ab,kw] OR inhalation [ti,ab,kw] OR inhalational [ti,ab,kw] OR volatile [ti,ab,kw]
#4 #2 AND #3
#5 TIVA [ti,ab,kw] OR propofol [ti,ab,kw] OR sevoflurane [ti,ab,kw] OR enflurane [ti,ab,kw] OR isoflurane [ti,ab,kw] OR desflurane [ti,ab,kw] OR halothane [ti,ab,kw]
#6 #1 OR #4 OR #5
#7 neoplasia [ti,ab,kw] OR neoplasias [ti,ab,kw] OR neoplasm [ti,ab,kw] OR neoplasms [ti,ab,kw] OR tumor [ti,ab,kw] OR tumors [ti,ab,kw] OR tumour [ti,ab,kw] OR tumours [ti,ab,kw] OR cancer [ti,ab,kw] OR cancers [ti,ab,kw] OR malignancy [ti,ab,kw] OR malignancies [ti,ab,kw]
#8 mortality [ti,ab,kw] OR survival [ti,ab,kw] OR "Kaplan-Meier" [ti,ab,kw] OR "proportional hazard model" [ti,ab,kw] OR "cox regression" [ti,ab,kw] OR "recurrence-free survival" [ti,ab,kw] OR "disease-free survival" [ti,ab,kw] OR recurrence [ti,ab,kw]
#9 #6 AND #7 AND #8.

Participant or population: All patients undergoing cancer surgery with intravenous or inhalation anesthesia.

Intervention: Propofol-based total intravenous anesthesia.

Comparator: Inhalation anesthesia.

Study designs to be included: Randomized-controlled trials and observational studies (prospective or retrospective).

Eligibility criteria: We intend to include all studies if they meet the following criteria: (1) randomized controlled trials (RCTs), observational studies (prospective or retrospective) that investigate the impact of anesthetic agents on long-term survival during cancer surgery; (2) patients undergoing resection of malignant neoplasm under general anesthesia; (3) comparing propofol-based intravenous anesthesia (TIVA) with inhalation anesthesia such as halothane, enflurane, isoflurane, sevoflurane or desflurane. (4) reporting overall survival (OS) or recurrence-free survival (RFS) or disease-free survival (DFS).

Information sources: We will systematically search the following electronic databases (PubMed, Medline, Embase, and the Cochrane Library) from inception to July 2022 for eligible studies. Any potentially relevant studies will be manually searched based on the references of the identified studies.

Main outcome(s): Overall survival and recurrence-free or disease-free survival.

Additional outcome(s): None.

Data management: Two reviewers (YX.T. and LL.T.) will independently extract data using a specially designed data checklist. Briefly, the following information are collected: (1) general information: study design, title, first author's name, publication year, country; (2) characteristics of participants: number of patients, age, American Society of Anesthesiologists (ASA) class, type of cancer, type of surgical procedure, elective or emergency nature of surgery, tumor staging; (3) interventions: anesthetic protocol in each group; (4) outcomes: follow-up time, the hazard ratio (HR) and 95% confidence intervals (95% CIs) of reported outcomes. Disagreements will be resolved through consensus or discussed with a third reviewer (B.C.).

Quality assessment / Risk of bias analysis: Two reviewers (YX.T. and YT.Y.) will assess the risk of bias of included studies independently. Disagreements will be resolved through consensus or discussed with a third reviewer (B.C.). The randomized control trials will be assessed using the Cochrane risk of bias assessment tool, while the Newcastle-Ottawa Scale (NOS) will be adopted for observational studies.

Strategy of data synthesis: Review Manager software 5.4. will be applied for meta-analysis. Adjusted Hazard ratios (HRs) and 95% confidence intervals (CIs) will be used to estimate the efficacy. We will consider inhalation anesthesia as the reference group. If the intravenous anesthesia group is considered as the reference, we will invert the HRs and CIs. Statistical heterogeneity will be evaluated by the Q statistics and I2 test. When P is less than 0.1 or I2 is greater than 50%, significant heterogeneity will be considered. In this case, a random-effects model will be applied; otherwise, a fixed-effects model will be conducted. P values less than 0.05 will be regarded as statistically significant. We will also evaluate publication bias by using funnel plots and Egger's regression asymmetry test. Trial sequential analysis (TSA) software 0.9.5.10 will be used to examine the reliability and conclusiveness of the available evidence.

Subgroup analysis: In order to explore the underlying origins of heterogeneity, subgroup analysis will be performed based on different types of cancer and inhalation anesthetics. If relevant data are available, subgroup analysis will be performed based on different surgical methods, cancer stages, and American Association of Anesthesiology status.

Sensitivity analysis: Sensitivity analyses will be performed to evaluate the stability of our conclusions by excluding low-quality studies, studies without matching baseline characterestics.

Language: English.

Country(ies) involved: China.

Keywords: intravenous anesthesia; propofol; inhalation anesthesia; survival; cancer.

Contributions of each author:

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