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Outcomes of cancer surgery after inhalational and intravenous anesthesia: A systematic review

Sinor Soltanizadeh, M.S. *, Thea H. Degett, M.D., Ismail Gögenur, DMSc

Center for Surgical Science, Zealand University Hospital, Lykkebækvej 1, DK-4600 Køge, Denmark

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ABSTRACT

Perioperative factors are probably essential for different oncological outcomes. This systematic review investigates the literature concerning overall mortality and postoperative complications after cancer surgery with inhalational (INHA) and intravenous anesthesia (TIVA).

A search was conducted according to the PRISMA guidelines, including studies with patients undergoing surgery for cancer and where TIVA was compared with INHA. Two investigators identified relevant papers in the databases: PubMed, Scopus, EMBASE and the Cochrane Library. Risks of bias assessment tools from the Cochrane Collaboration were used for evaluating quality of evidence. Eight studies with a total of 10,696 patients were included. Four studies reported data regarding overall mortality and four studies reported data regarding postoperative complications. Evidence was evaluated to be of moderate to serious risk of bias. Three retrospective studies presented a hazard ratio (HR) adjusting for several confounders. One study reported an increased overall mortality after INHA with a HR of 1.47 (95% CI 1.31–1.64, $p \leq 0.001$), while another study reported a tendency of decreased overall mortality after TIVA (HR 0.85, 95% CI 0.72–1.00, $p = 0.051$). A third study showed no difference in the overall mortality, but prolonged recurrence-free survival after TIVA with a HR of 0.48 (95% CI 0.27–0.86, $p = 0.014$). In one study, the rate of pulmonary complications was significantly higher after INHA compared with TIVA, while other postoperative complications were comparable.

There are currently four propensity-adjusted retrospective studies indicating that TIVA might be the preferred anesthetic choice in cancer surgery. However, evidence is currently of low quality and randomized clinical trials are required for further investigation.

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* Corresponding author at: Strandboulevarden 10, 4-1, DK-2100 Copenhagen, Denmark.
E-mail addresses: sinso@regionsjaelland.dk (S. Soltanizadeh), thhd@regionsjaelland.dk (T.H. Degett), igo@regionsjaelland.dk (I. Gögenur).

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1. Introduction

Overall cancer mortality in breast, colorectal, and uterine cancer, has shown a moderate decline through the years 2000 to 2010 probably due to early diagnostics and better access to treatment [1]. With the optimization of surgical procedures, cancer surgery has become more advanced leading to shorter hospital stays and fewer postoperative complications [2,3]. However, a high proportion of patients still have recurrence after surgery with curative intent [4–6].

Various factors in the perioperative period, including the inflammatory and endocrine metabolic stress response are suggested to promote a micro metastatic process, which results in poor long-term oncologic outcomes [7]. In general anesthesia, it is suggested that inhalational anesthesia (INHA) such as sevoflurane and isoflurane may modulate anti-metastatic immunity by inhibiting NK cell cytotoxicity and inhibit T-helper cell proliferation [8]. This could potentially be unfavorable for cancer survival. In contrast, propofol-based total intravenous anesthesia (TIVA) is suggested to have anti-inflammatory features and to be advantageous compared with INHA by promoting the activation of T-helper cells, decreasing matrix metalloproteinases, and not suppressing NK cell activity to the same extend as INHA [9–12]. The immunological impact of the anesthetic agents may thus influence clinical measures including overall mortality and postoperative recovery.

The aim of this systematic review was to investigate if there is a difference in overall mortality and postoperative complications in patients receiving INHA versus TIVA during cancer surgery.

2. Materials and methods

This systematical review was conducted according to the PRISMA guidelines with adherence to all items except for #15, #16, #21 and #23, which are required for the conduction of meta-analysis [13], which was not possible to conduct with the current studies.

2.1. Eligibility criteria

The study question was structured according to PICO. Population: patients undergoing cancer surgery. Intervention: primary cancer surgery with either INHA or TIVA. Comparison: TIVA versus INHA. Outcome: overall mortality and postoperative complications. All human studies meeting the PICO criteria were eligible for inclusion. Language was limited to English, French, German, Spanish and Scandinavian languages. No limitations were set on study design or publication year. The exclusion criteria were: animal studies, in vitro studies and anesthetic interventions in combination with other simultaneous interventions.

2.2. Study collection and selection

A systematic search was conducted in PubMed, Scopus, EMBASE, and the Cochrane Library, recently updated the 12th of March 2017. The search was modified for each database; hence, mesh words were only added in databases with mesh terms.

PubMed example*((((((((((((((((remifentanil) OR propofol) OR infusional) OR infusion) OR iv) OR TIVA) OR intravenously) OR intravenous) OR "Propofol"[Mesh]) OR "remifentanil" [Supplementary Concept]) OR "Anesthesia, Intravenous"[Mesh]) OR "Anesthetics, Intravenous"[Mesh])) AND ((((((((((((((((sevoflurane) OR gas) OR insufflation) OR volatile) OR inhalational) OR inhalation) OR INHA) OR "sevoflurane" [Supplementary Concept]) OR isoflurane) OR "Isoflurane"[Mesh]) OR desflurane) OR "desflurane" [Supplementary Concept]) OR "Anesthesia, Inhalation"[Mesh]) OR "Anesthetics, Inhalation"[Mesh]) OR halothane) OR "Halothane"[Mesh]))) AND ((((((((((("Surgical Procedures, Operative"[Mesh]) OR "General Surgery"[Mesh]) OR operations) OR surgeries) OR procedures) OR procedure) OR operation) OR operative) OR surgical) OR surgery))) AND ((((((((((("Neoplasms"[Mesh]) OR tumors) OR tumor) OR malignancy) OR malignant) OR malign) OR neoplasms) OR neoplasm) OR cancer))) AND ((((((((((((("Anesthetics, General"[Mesh]) OR "Anesthetics"[Mesh]) OR "Anesthesia, General"[Mesh]) OR "Anesthesia"[Mesh]) OR anaesthesiology) OR anesthesiology) OR anaesthetics) OR anesthetics) OR anaesthetic) OR anesthetic) OR anaesthesia) OR anesthesia))*

Covidence.org was used as a tool to screen records for eligibility, and duplications were removed manually. Two investigators screened abstracts and titles of all articles independently. After the primary screening, articles were full-text screened and discussed between two investigators. Conflicts were evaluated in consensus with a third investigator. One investigator additionally screened references of included studies, and all studies cited by the included studies were screened in SCOPUS.

2.3. Data collection

The following data were extracted for demographic characteristics of studies: year of participant enrolment, study design, number of patients in each intervention group, distribution of gender, mean age, anesthetic agents used in each intervention group, and primary cancer site. Overall mortality was defined by any cause of death after the patient was surgically treated. From each study the hazard ratio (HR) regarding overall mortality and the recurrence-free period were retrieved. Postoperative complications were categorized into organ related complications and in-hospital death. Cardiovascular complications included arrhythmia, deep venous thrombosis, pulmonary embolism, changes in ECG or cardiac enzyme, or stenosis. Respiratory complications included atelectasis, respiratory failure, pneumonia or pulmonary edema. Neurological complications included transient ischemic attack, stroke, delirium, or cerebral edema. Infectious complications included surgical site related infections, urinary tract infections, sepsis or septic shock, clostridium difficile, or diarrhea. Gastrointestinal complications included bleeding, ileus, anastomotic leak, enterocutaneous fistula, or vomiting. Renal, hematological and multisystem organ were presented as reported in included studies.

Missing data were attempted to be collected through correspondence with the authors.

2.4. Evaluation of evidence

As there is currently no risk of bias assessment tools available for both observational and randomized studies, two different tools from the Cochrane Collaboration were used in this review [14,15]. Bias in non-randomized studies were evaluated with ACROBAT-NRSI (A Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Intervention), a validated quality assessment tool based on following