International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Long-Term Outcomes after Use of Perioperative Glucocorticoids in Patients Undergoing Cancer Surgery

INPLASY2023120015

doi: 10.37766/inplasy2023.12.0015

Received: 03 December 2023

Published: 03 December 2023

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ADMINISTRATIVE INFORMATION

Support - NA.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023120015

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 December 2023 and was last updated on 03 December 2023.

INTRODUCTION

Review question / Objective The population of interest being humans at 18 years or older undergoing elective surgicaltreatment for cancer of any kind. The intervention of interest was administration of single or repetitivedoses of glucocorticoids during the perioperative period which was defined as the time rangingfrom one week prior to surgery until 30 days after. Studies investigating topical, intramuscularor inhalational glucocorticoids were excluded. If glucocorticoids were administered as part of ananti-hormone therapy regime; as chemotherapy; or as premedication before chemotherapy, trials wereexcluded. So were trials including patients with hypothalamic pituitary adrenal (HPA) axis dysfunctionor long-term glucocorticoid treatment close to the time of surgery. The exposure to perioperativeglucocorticoids should be compared to control groups either receiving placebo; standard of care; nointervention; or another intervention.The outcomes of interest evaluated the long-term safety and potential benefits of oral or intravenousperioperative glucocorticoids for cancer surgery. The primary outcome, recurrence, was a composite oflocal, regional, and distant recurrence. OS was defined as time from surgery to death of any cause;DFS, also called relapse-free survival or recurrence-free survival, was defined as the time from surgeryuntil death of any cause or cancer recurrence; and CSS was defined as the time from surgery to deathfrom the same cancer. A follow-up time of at least six months after surgery was required.

Condition being studied The global disease burden of cancer is considerable with as much as 18 million new cases annually, and more than half as many mortalities in 2018. The majority of cancer

deaths are caused by metastases, and the numbers are expected to nearly double in 2040. Surgical resection remains the primary curative treatment of solid cancers.
Glucocorticoids are known to modulate the inflammatory stress response and are increasinglyused in the perioperative period.Administration of low-dose perioperative dexamethasone is used forprevention of postoperative nausea and vomiting (PONV). Use of high dose glucocorticoids has beenshown to have analgesic effects and may even decrease the risk of postoperative complications without increasing short-term adverse events.

METHODS

Participant or population The population of interest being humans at 18 years or older undergoing elective surgicaltreatment for cancer of any kind.

Intervention The intervention of interest was administration of single or repetitive doses of glucocorticoids during the perioperative period which was defined as the time ranging from one week prior to surgery until 30 days after.

Comparator The exposure to perioperative glucocorticoids should be compared to control groups either receiving placebo; standard of care; nointervention; or another intervention.

Study designs to be included Retrospective cohort study; randomized controlled trial.

Eligibility criteria Studies investigating topical, intramuscularor inhalational glucocorticoids were excluded. If glucocorticoids were administered as part of an anti-hormone therapy regime; as chemotherapy; or as premedication before chemotherapy, trials were excluded. So were trials including patients with hypothalamic pituitary adrenal (HPA) axis dysfunctionor long-term glucocorticoid treatment close to the time of surgery.

Information sources Pubmed; Web of science ; Embase.

Main outcome(s) Recurrence.

Additional outcome(s) Overall survival (OS); disease-free survival(DFS); and cancer-specific survival (CSS).

Quality assessment / Risk of bias analysis Risk of bias assessment for randomised studies was performed using the Cochrane Risk of Biastool 2.0 (RoB 2.0).
Risk of bias for non-randomised studies was assessed using the Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis For each outcome, events and sample size for postoperative year one, three and five were extractedas well as HR and 95% confidence interval (CI). The extracted events were as follows: cancer recurrence for the primary outcome recurrence; death from any cause for OS; death of any cause or cancer recurrence, whichever came first, for DFS; and death from the same cancer for CSS.Frequency meta-analyses of extracted event measures were performed by applying a randomeffect model (inverse variance) calculating risk ratios and 95% CI using the software tool RevMan5.3 . The DerSimonian-Laird (DL) tau2 estimator was applied and heterogeneity was assessed by Chi2 testing and I2 statistics. Time-to-event meta-analyses of extracted hazard-ratios were performed by applying a randomeffect model (inverse variance) calculating HR using the statistics program R-studio and applyingthe packages meta, metagen and metafor.

Subgroup analysis The impact of the following factors on outcomes were pre-specified as subgroup analyses ofinterest: glucocorticoid type; timing in relation to surgery, frequency and dose of the glucocorticoid administration; cancer type; and time and magnitude of the surgery. It was also pre-specified that afixed effect model would be applied on analyses were I2was below 20%.

Sensitivity analysis The Sidik-Jonkman estimator for tau2 was applied withHartung-Knapp adjustment in the given random effect model. Prediction intervals were calculatedto provide estimates of the expected effect size of future studies based on current evidence. Heterogeneity was assessed by Chi2 testing and I2 statistics. Publication bias was assessed by Egger's test, and funnel plots of unadjusted and adjusted OS hazard-ratios were created for visualinspection.

Country(ies) involved China.

Keywords oncoanaesthesiology; surgery; anesthesiology; cancer; perioperative treatment; steroids;corticosteroids; glucocorticoids; recurrence; survival.

Contributions of each author
Author 1 - yunkui zhang.
Author 2 - yuecheng yang.
Author 3 - jun zhang.