# INPLASY PROTOCOL

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Conflicts of interest: None declared.

## INTRODUCTION

Review question / Objective: (1) the study subjects were diagnosed with non-muscleinvasive bladder cancer and underwent transurethral resection of bladder tumor under regional anesthesia or general anesthesia; (2) Patients in the intervention

Effect of regional versus general anesthesia on recurrence of non-muscle invasive bladder cancer: a systematic review and meta-analysis

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Review question / Objective: (1) the study subjects were diagnosed with non-muscle-invasive bladder cancer and underwent transurethral resection of bladder tumor under regional anesthesia or general anesthesia; (2) Patients in the intervention group only received regional anesthesia; (3) Patients in the control group received general anesthesia; (4) The cancer recurrence rate, recurrence time and cancer progression were compared between the two groups.(5)The study types were prospective or retrospective cohort studies or randomized clinical trials.

Condition being studied: Non-muscle-invasive bladder cancer (NMIBC) is the most common type of bladder cancer, accounting for about 75%. Transurethral resection of bladder tumor (TURBT) is the primary treatment for NMIBC. Depending on the tumor's histological grade and TNM stage, the surgeon will determine whether further adjuvant therapy, including intravesical chemotherapy and BCG immunotherapy, is needed following TURBT surgery. NMIBC is prone to recurrence and disease progression, with a 5-year recurrence rate of 50 to 70%.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 November 2022 and was last updated on 20 November 2022 (registration number INPLASY2022110097).

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### **METHODS**

Search strategy: ((("Anesthesia, Conduction"[Mesh]) OR ((((((Anesthesia, Regional) OR (Anesthesia, Epidural)) OR (Anesthesia, Caudal)) OR (Anesthesia, Local)) OR (Anesthesia, Spinal)) OR (Nerve Block)) OR (Autonomic Nerve Block + **Brachial Plexus Block Cervical Plexus** Block))) AND (("Anesthesia, General"[Mesh]) OR ((((Anesthesia, Inhalation) OR (Anesthesia, Closed-Circuit)) OR (Anesthesia, Endotracheal)) OR (Anesthesia, Rectal)) OR (Balanced Anesthesia)))) AND ((("Urinary Bladder Neoplasms"[Mesh]) (Urinary Bladder Neoplasm)) OR (Bladder Tumors)) OR (Bladder Tumor)) OR (Tumor, Bladder)) OR (Tumors, Bladder)) OR (Neoplasms, Bladder)) OR (Bladder Neoplasms)) OR (Bladder Neoplasm)) OR (Neoplasm, Bladder)) OR (Urinary Bladder Cancer) OR (Cancer, Urinary Bladder)) OR (Malignant Tumor of Urinary Bladder)) OR (Cancer of the Bladder)) OR (Bladder Cancer)) OR (Bladder Cancers)) OR (Cancer, Bladder)) OR (Cancer of Bladder)))).

Participant or population: Patients were diagnosed with NMIBC and underwent TURBT under regional anesthesia or general anesthesia.

Intervention: Patients in the intervention group only received RA.

Comparator: Patients in the control group received GA.

Study designs to be included: Prospective or retrospective cohort studies or randomized clinical trials.

Eligibility criteria: (1) non-bladder cancer patients or combined with other tumors; (2) patients receiving more than one type of anesthesia; (3) Lack of comparison of tumor recurrence rate between the control group and the experimental group; (4) Reviews, letters, comments, author responses, and case reports were excluded.

Information sources: PubMed, Embase, Web of Science, the Cochrane Library and China National Knowledge Infrastructure

Main outcome(s): Cancer Recurrence rate, time to recurrence and progression.

Quality assessment / Risk of bias analysis: Newcastle-Ottawa Scale (NOS) was used to test the methodological quality and risk of bias of the included prospective or retrospective cohort studies. This 9-point scale assesses bias in three aspects: selection of study subjects, comparability between groups, and ascertainment of exposure or outcome. Studies with a score of over 7 were considered to be of high quality.

Strategy of data synthesis: Relative risk (RR), hazard ratios (HR), standardized mean difference (SMD), and 95% confidence levels (CI) were used to compare the strength of the association between RA versus GA and NMIBC recurrence rate, time to recurrence, progression, and overall survival. The fixed effects model (FEM) and random effects model (REM) were used to calculate pooled RRs and HRs. The Chi-square-based Q-test and I2 test were adopted to assess heterogeneity between studies. When the P of the Q-test was over 0.05 or 12 <50%, FEM was used; otherwise, REM was applied. In addition, subgroup analysis was conducted according to the specific type of RA and the risk of bladder cancer to

explore their potential impact on the study results. We applied sensitivity analysis to test the stability and credibility of the results by eliminating each study one by one. Begg's funnel plot and Egger's test were used to estimate publication bias. We used Stata software (version 12.0) and Review Manager (Version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) to perform this meta-analysis.

Subgroup analysis: Subgroup analysis based on the type of RA detected a significant association between spinal anesthesia and lower recurrence rates of NMIBC whereas similar results were not found in patients who received epidural anesthesia. When we performed subgroup analyses according to risk stratification of NMIBC, the use of RA was significantly associated with a lower recurrence rate in high-risk NMIBC. The choice of anesthesia type did not affect the recurrence rate of low-risk NMIBC.

Sensitivity analysis: Sensitivity analysis was adopted to assess the reliability of this meta-analysis and to estimate the impact of each article on the combined results by sequentially removing each included individual study. The combined results of our study were reliable, with no single data significantly affecting the pooled SMD, RR or HR

Language restriction: English, Chinese.

Country(ies) involved: China.

Keywords: Anesthesia, General; Anesthesia, Conduction; Urinary Bladder Neoplasms; Recurrence.

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