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ADMINISTRATIVE INFORMATION**Support** - No support.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202630090**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 March 2026 and was last updated on 24 March 2026.**INTRODUCTION**

Review question / Objective Upper tract urothelial carcinoma (UTUC) is a potentially lethal disease, the standard management of UTUC is radical nephroureterectomy with bladder cuff excision, reported intravesical recurrence (IVR) rate after RNU is thought to be 22% to 47%. The aim of study was to identify significant risk factors of IVR from a systematic review and meta-analysis.

Rationale In this meta-analysis we aim to determine the possible factors of postoperative intravesical recurrence (IVR) in patients with UTUCs. The purpose of this study is to offer preliminary insights into the possibility of implementing individualized treatments based on patient risk stratification.

Condition being studied An increasing number of studies have focused on risk factors for IVR after RNU, proposed risk factors include some patient-related factors (male, sex, history of bladder cancer, and preoperative chronic kidney disease

[CKD], etc.), tumor-specific factors (preoperative urine cytology, ureteral location, multifocality, invasive pathologic T stage, and tumor necrosis, etc.), and treatment-specific factors (laparoscopic approach, extravesical bladder cuff removal, and positive surgical margins, Intravesical Instillation, etc.). However, the results have been controversial with limited evidence, our purpose was to assess significant predictors of IVR after RNU for UTUC from a systematic review to establish surveillance strategies. Patients diagnosed with BCa after RNU with bladder cuff excision to treat UTUCst.

METHODS

Search strategy Two authors (GY.W. and J.G.) together performed a computerized bibliographic search of the PubMed, Embase, and Web of science, using combinations of the following search terms ("upper tract" OR "upper urinary tract" OR "renal pelvis" OR "ureter") AND ("urothelial carcinoma" OR "transitional cell carcinoma" OR "carcinoma" OR "cancer") AND ("Nephroureterectomy") AND ("Bladder" OR

"intravesical recurrence"), in addition, only "Humans" and "English language" filters were applied without a time period restriction.

Participant or population Patients with bladder tumors (Bca).

Intervention Radical nephroureterectomy (RNU) with bladder cuff excision (BCE) to treat UTUCs.

Comparator Patients without bladder tumors (Bca) who received radical nephroureterectomy (RNU) with bladder cuff excision (BCE) to treat UTUCs.

Study designs to be included Studies were included to this meta-analysis if they compared patients diagnosed with BCa (P) after RNU with bladder cuff excision to treat UTUCs (I) to patients without previous/synchronous bladder tumor (C) to determine independent clinicopathologic risk factors of IVR (O) using multivariate logistic regression analysis.

Eligibility criteria (1) Only large studies that included more than 100 patients who had been treated with RNU, rather than conservative surgery.

(2) Only studies defined IVR as a pathologically confirmed occurrence in the urinary bladder following RNU, the follow-up time was more than 1 year.

(3) Studies were excluded which contained patients who had a previous or synchronous bladder cancer.

(4) Only studies that provided hazard ratios (HRs) with their corresponding 95% CIs, or HR and 95%CIs can be estimated according to provided data.

Information sources Computerized bibliographic search of the PubMed, Embase, and Web of science.

Main outcome(s) Independent clinicopathologic risk factors of IVR (intravesical recurrence), such as gender, tumor location, Pathological T stage, Pathological N stage, tumor grade, tumor multifocality, Lymphovascular invasion (LVI), Preoperative urine cytology, ureteroscopy, Positive surgical margins, Intravesical instillation for final evaluation.

Quality assessment / Risk of bias analysis Two independent reviewers (GY.W. and J.G.) evaluated each included studies by means of the Newcastle–Ottawa scale (NOS), and when there were divergences, they discussed them or judged by

other reviewers. The NOS assessed studies based on three aspects: selection, comparability of groups, and outcomes. The risk of confounding bias was high (red) if the confounder was not reported or not balanced among the treatment groups, without any adjustment in the statistical analysis. Alternatively, the risk of confounding bias was low (green) if the confounder was reported and balanced or adjusted for in the statistical analysis. Otherwise, the risk was considered to be unclear (yellow). Each study is eligible for a maximum of 9 points under the NOS guidelines, and studies with an NOS score 7-9 were evaluated of high quality, score 4-6 were evaluated of medium quality, and score ≤ 3 were evaluated of low quality.

Strategy of data synthesis The Cochran's chi-squared test and the I² statistic were used to quantitatively evaluate heterogeneity and measure the percentage of volatility among the selected studies.

Subgroup analysis Our meta-analysis chose some main acknowledged factors, such as gender, tumor location, Pathological T stage, Pathological N stage, tumor grade, tumor multifocality, Lymphovascular invasion (LVI), Preoperative urine cytology, ureteroscopy, Positive surgical margins, Intravesical instillation for final evaluation.

Sensitivity analysis If the heterogeneity P-value was 50%, a significant heterogeneity existed, which also leading to a random-effects model was used rather than the fixed-effect model, otherwise a fixed effect model was used.

The meta-analysis was performed for each potential factor for IVR using the predictor effect (PE) and its standard error (sePE)[13], Log HR and variance were extracted from included studies and synthesized. For each study, HRs for survival with corresponding 95% CIs were analyzed in terms of the impact of IVRs following RNU on oncologic outcomes. Meta-analyses and forest plots were performed using Stata 18.0 software.

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Language restriction Only English language.

Country(ies) involved China (China-Japan Union Hospital of Jilin University).

Keywords Urinary tract; Urothelial carcinoma; Nephroureterectomy; Intravesical recurrence.

Contributions of each author

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