

Review

Radical nephroureterectomy versus endoscopic procedures
for the treatment of localised upper tract urothelial
carcinoma: A meta-analysis and a systematic review
of current evidence from comparative studies



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Abstract

The conservative management of upper tract urothelial carcinoma (UTUC) has seen important developments over the last 10 years with advances in endoscopy. Our aim was to compare the available evidence regarding the impact of endoscopic nephron sparing procedures (NSP) and radical nephroureterectomy (RNU) on survival of upper tract urothelial carcinoma (UTUC). A critical review of Pubmed/Medline, Embase and the Cochrane Central Register of Controlled Trials was performed in July 2013 according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement. Overall, eight publications were selected for inclusion in this meta-analysis but all of them were retrospective or non-randomised comparative studies. The primary end points were the overall and cancer-specific survivals (OS and CSS) in the two treatment groups. We achieved to pool data on 1002 patients diagnosed with localised UTUC and treated either by endoscopic NSP ($n = 322$) or by RNU ($n = 680$). No significant difference was found in terms of OS and CSS between RNU and endoscopic NSP (HR = 1.47 and $p = 0.31$; HR = 0.96 and $p = 0.91$, respectively). However, the low level of evidence (3b) and the heterogeneity of the studies limited the quality of the results. In the absence of prospective and randomised studies, the equivalent oncologic control for endoscopic NSP and RNU is not provided by this meta-analysis. Multicentre prospective studies are urgently needed to assess the oncologic outcomes of UTUC with endoscopic management. In the next multicentre studies, the patients should be matched on the basis of the tumour stage (imaging) and grade (biopsy) at diagnosis.

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Introduction

Upper tract urothelial carcinomas (UTUCs) are rare tumours with an incidence rate of 1.45–2.06 cases per 100,000 person-years that represent only 5–10% of urothelial carcinomas.^{1,2} According to the 2013 European Association of Urology guidelines, radical nephroureterectomy (RNU) with bladder cuff still remains the gold standard

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treatment for patients with UTUC.³ Despite the oncological efficacy of this radical approach, it is associated with morbidity and loss of nephron units.

The primary use for the direct macroscopic evaluation and biopsies of the lesions through endoscopic management (i.e., ureterorenoscopy [URS] or percutaneous nephroscopic resection of the tumour [PNRT]) is of growing interest as a treatment strategy for UTUCs.³ Primarily reserved for imperative indications, the advances in endourologic techniques and materials have led to first-line nephron-sparing procedures (NSP) for selected patients.

Some authors have reported the technical feasibility and safety of the endoscopic NSP for UTUCs. It is now admitted that endoscopic procedures are both cost effective and less morbid than the radical approach.⁴ However, due to the rarity of these tumours, the oncological efficacy of the endoscopic NSP has not been definitively proven. Several researchers have described excellent oncologic control in terms of cancer specific and overall survivals, at the cost of a recurrence rate of 6.2–88% assessed during close follow-up.^{5–12} However, these studies are often retrospective and include a small number of patients.

Furthermore, there is paucity in literature regarding reports comparing the oncological results of endoscopic NSP with those of RNU. Prospective randomised studies are notably lacking today. Accordingly, we performed a meta-analysis to evaluate the oncological efficacy of the endoscopic treatment of UTUCs.

Methods and evidence acquisition

Search strategy

A systematic review of electronic databases (i.e., PubMed, Embase and the Cochrane Central Register of Controlled Trials) was achieved according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement guidelines.

The search strategy was adapted to each database. No language restriction was applied. Reference lists of all identified papers were screened to identify additional potentially relevant citations. The literature search included studies published up to July 2013.

Inclusion and exclusion criteria

All articles were assessed for eligibility using predefined criteria. Our search was limited to randomised or observational controlled studies published as a full paper or abstract.

Intervention: open or laparoscopic radical nephroureterectomy and ureteroscopic or percutaneous surgery for UTUC.

Population: adult patients diagnosed with UTUC treated by surgery.

Outcomes: overall survival (OS) and cancer specific survival (CSS) were considered as primary outcomes.

Recurrence-free survival (RFS) was considered as a secondary outcome.

The following studies were excluded: studies comparing partial ureterectomy, endoscopic studies without surgery, and studies without direct comparison groups (single-arm studies).

Data extraction

A standardised pre-piloted data extraction sheet was used. All titles and abstracts identified by the search strategy were screened. Only citations which were clearly irrelevant were excluded at this stage. All potentially eligible studies were obtained for full text screening. The extracted information included: study location, characteristics and design, patient demographics, details regarding intervention and control, outcomes and timing of outcomes, study methodology, eligibility, loss during follow-up, and indicators of study bias.

Statistical analysis

We completed a narrative synthesis of the findings from the included studies regarding the intervention and outcomes. Summaries of intervention effects for each study were provided using available data and especially Hazard Ratios (HR) that remain the most appropriate statistic to analyse time-to-event data (survival). Available HR and their variances were extracted directly from the published results. Non-available HR and their variances were calculated using an Excel spread sheet developed by Tierney et al.¹³ after indirect extraction of either available summary statistics (observed events, expected events, variance, confidence intervals, *p*-values) or data from Kaplan–Meier curves using the methods described by Parmar et al.¹⁴ However, to occasionally replace HR that could not be estimated from published data, we used the available dichotomous data from the trials for the number of deaths per treatment group at a specified time point.

Meta-analyses of pooled data were conducted using a random-effects model and the inverse variance method. Statistical heterogeneity was assessed by Chi^2 and I^2 test. The scale of I^2 values ranges between 0% and 100%, with higher values denoting a greater degree of heterogeneity. Two-tailed $p < 0.05$ was considered statistically significant. The data were analysed with Review Manager (RevMan) 5.1 which was developed by the Cochrane Collaboration.

Evidence synthesis

Quality of the comparative studies and level of evidence

The full process of the systematic literature review is shown in Fig. 1. According the PRISMA search strategy, we identified 75 articles in Medline, Embase, and the

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