



Review article

Urethral recurrence after radical cystectomy for urothelial carcinoma: A systematic review and meta-analysis

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Abstract

Purpose: Currently, identified factors for urethral recurrence (UR) are based on individual reporting which has displayed controversy. In addition, risk of UR is one of the limiting factors to offer neobladder diversion during radical cystectomy (RC). We aim to systematically evaluate the incidence and risk factors of UR post-RC and its effect on survival.

Materials and methods: A systematic online search was conducted according to PRISMA statement for publications reporting on UR after RC. From initial 802 results, 14 articles including 6169 patients were included finally after exclusion of ineligible studies.

Results: The incidence rate of UR was 4.4% (1.3%–13.7%). It was significantly lower with neobladder diversion (odds ratio = 0.44, 95% CI: 0.24–0.79, $P = 0.006$). Muscle invasion (hazard ratio = 1.18, 95% CI: 0.86–1.62, $P = 0.31$), carcinoma in situ (hazard ratio 0.97, 95% CI: 0.64–1.47, $P = 0.88$), prostatic stromal involvement (hazard ratio = 2.26, 95% CI: 0.01–627.75, $P = 0.78$), and prostatic urethral involvement (hazard ratio = 2.04, 95% CI: 0.20–20.80, $P = 0.55$) have no significant effect on UR. Men displayed tendency toward higher incidence of UR (odds ratio = 2.21, 95% CI: 0.96–5.06, $P = 0.06$). Absence of recurrence displayed tendency toward better disease specific survival, yet not significant (hazard ratio = 0.84, 95% CI: 0.66–1.08, $P = 0.17$). These results are limited by the retrospective nature of the included studies.

Conclusion: Muscle invasion, carcinoma in situ and prostatic stromal or urethral involvement at time of RC have no significant effect on UR. Orthotopic neobladder is associated with a significant lower risk of UR after RC. © 2017 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Neobladder; Radical cystectomy; Urethral recurrence; Urothelial carcinoma

1. Introduction

Urothelial carcinoma is the most common type of bladder cancer, which can affect also the whole urinary tract lining urothelium [1]. Currently, radical cystectomy (RC) is the gold standard treatment for muscle invasive bladder cancer [2,3], yet recurrence of the disease in the remnant urothelium is possible [4]. Popularity of urinary diversion using orthotopic neobladder (ONB) is increasing due to its favorable functional outcomes and better quality of life [5,6]. However, expected higher risk of urethral

recurrence (UR) in some patients limits urologists to offer ONB to these patients.

1.1. In the literature, the impact of prostatic involvement by urothelial tumor on UR is controversial.

Some authors reported that prostatic involvement is associated with high risk of UR [7–9]. Although others reported that ONB should not be prohibited based on prostatic involvement [10] other factors like involvement of bladder neck, multifocality, and carcinoma in situ (CIS) were reported to be associated with higher risk of UR [11–13]. However, this data is based mainly on individual reporting with no comprehensive analysis available until now.

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For this, we conducted a systematic review and meta-analysis to reassess the factors associated with a significant risk of UR and how UR can affect the patients' survival.

2. Methods

2.1. Search strategy

According PRISMA statement [14], systematic online search was conducted through online data bases (PubMed, Wiley online library and Cochrane databases). The following keywords were used as bladder cancer, RC, and UR. Initial assessment of all retrieved results was performed with subsequent exclusion of the unrelated articles and review articles. Eligible publications were subjected to full-text assessment including a manual search in their reference lists. Publications which met one of the following criteria were excluded as (1) no reported data on UR. (2) Series including patients undergoing RC for nonurothelial carcinomas (squamous carcinoma, adenocarcinoma, and other rare histological entities) (3) reports on urothelial recurrence including upper tract with irretrievable data on UR (IV) repeated publications for the same authors.

2.2. Data extraction

The following variables were extracted as number of the patients who underwent RC, gender, age, duration of follow-up, type of urinary diversion, incidence of UR, gender of recurrent cases, type of diversion in recurrent cases and hazard ratio (HR) and 95% CI for the following factors based on multivariate analysis: BC stage, CIS, prostatic stromal involvement by tumor at time of cystectomy, and prostatic urethral involvement. HR and 95% CI for the effect of UR on disease specific survival (DSS) was extracted from Kaplan-Meier curves using the Tierney's method [15]. Data were extracted independently by 2 authors, then double-check was performed for accuracy.

2.3. Outcome measures

The primary outcome of this analysis was the effect of BC stage, CIS, urinary diversion, gender, prostatic stromal, and urethral involvement on the UR, and the effect of UR on DSS.

2.4. Statistical analysis

This meta-analysis was conducted using Review Manager (RevMan) software version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen). Log HR and standard error of the extracted HR were used in the pooled analysis of the examined factors. Odds ratio was used in analysis of the factors reported as dichotomous data (gender and diversion type). Random effect model was used

regardless I^2 value to minimize the effect of heterogeneity between the included studies.

3. Results

3.1. Search results and patient criteria

A total of 14 publications were included in this study after application of exclusion criteria [7,8,13,16–26]. The selection process is demonstrated in a CONSORT diagram (Fig. 1). A total number of 6,169 patients (5,335 men and 834 women) who underwent RC for urothelial BC were involved in the pooled analysis. A 2,607 (42.25%) patients had urinary diversion with ONB; yet 3,541 (57.40%) patients had non-ONB diversion. Diversion type was missed in 21 (0.34%) patients [13]. Overall, incidence of UR was 4.38% with a range between 1.3% [18] and 13.7% [16]. The summary of the included studies is provided in the Table.

3.2. Factors for UR

3.2.1. Gender

The incidence of UR in men was 164/3291 (4.99%). Among 709 women 10 developed UR (1.41%) [13, 16–18,20,23,26]. Despite obvious lower incidence in women, the difference was not significant. Odds ratio for UR in men to women was 2.21 (95% CI: 0.96–5.06) ($Z = 1.87$, $P = 0.06$, Fig. 2A).

3.2.2. Diversion

UR was significantly less in patients with ONB. In 1,615 patients with ONB, UR was detected in 36 patients (2.2%). In contrast, UR in patients with non-ONB was 174/3,136 (5.55%) [7,14,18–20,22,25,26]. Odds ratio for UR after ONB was 0.44 (95% CI: 0.24–0.79) ($Z = 2.73$, $P = 0.006$, Fig. 2B).

3.2.3. Stage of BC

Presence or absence of histologically confirmed muscle invasion at time of cystectomy had no effect on UR. HR for

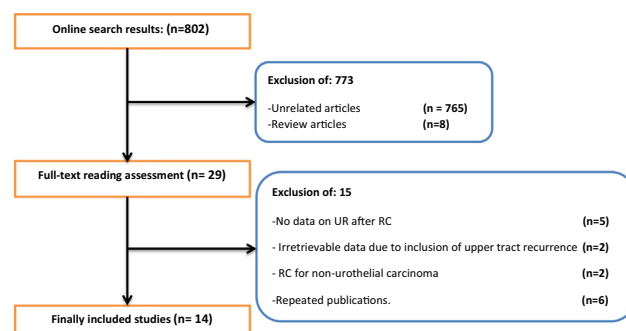


Fig. 1. CONSORT diagram illustrates the selection process of studies included in this meta-analysis. (Color version of the figure available online.)

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