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**ONCOLOGY/RECONSTRUCTION
REVIEW**

**Squamous cell carcinoma of the urinary bladder:
Systematic review of clinical characteristics and
therapeutic approaches**



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KEYWORDS

Squamous cell carcinoma (SCC);
Bladder;
Bilharzial;
Radical cystectomy;
Radiotherapy

ABBREVIATIONS

B-SCC, bilharzial-associated SCC;
CISC, clean

Abstract Objective: To highlight the current understanding of the epidemiology, clinicopathological characteristics, and management of squamous cell carcinoma (SCC) of the bladder, as it accounts for 2–5% of bladder tumours, with a focus on non-bilharzial-associated SCC (NB-SCC). The standard treatment for bladder SCC remains radical cystectomy (RC). We present an updated clinical profile of bladder SCC and a review of NB-SCC therapeutic approaches, including RC, neoadjuvant and adjuvant treatments, radiotherapy, chemotherapy, and immunotherapy.

Methods: Using search terms relating to SCC, urinary bladder, and treatment modalities, we performed a search of the PubMed and Embase databases to identify NB-SCC treatment approaches and outcomes. Peer-reviewed English language reports from 1975 to present assessing SCC management were included. Two authors independently screened and extracted the data.

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intermittent self-catheterisation;
 COX-2, cyclooxygenase 2;
 DFS, disease-free survival;
 FGF-2, fibroblast growth factor 2;
 HER-2, human epidermal growth factor receptor 2;
 HPV, human papilloma virus;
 LVI, lymphovascular invasion;
 LN, lymph node;
 NAC, neoadjuvant chemotherapy;
 NB-SCC, non-bilharzial SCC;
 OS, overall survival;
 PD-1, programmed cell death 1;
 PD-L1, programmed death-ligand 1;
 RC, radical cystectomy;
 SCC, squamous cell carcinoma;
 SCI, spinal cord injury;
 SEER, Surveillance, Epidemiology, and End Results

Results: Of the 806 articles screened, 10 met the pre-defined inclusion criteria. RC was performed in seven of the 10 studies. Although radiotherapy alone yielded poor outcomes, preoperative radiotherapy and RC were associated with improved survival. There is little evidence supporting the use of chemotherapy in NB-SCC, and its efficacy in relation to RC is not known.

Conclusion: Based on current literature, there is insufficient evidence to provide a treatment recommendation for NB-SCC. Whilst RC is the standard of care, the role of preoperative radiotherapy should be revisited and compared to RC alone. Additional studies incorporating multimodal approaches, contemporary radiation techniques, and systemic therapies are warranted. Immunotherapy as a treatment for bladder SCC has yet to be investigated.

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Introduction

Bladder cancer is the most common malignancy of the urinary tract, accounting for ~77,000 new cases and 16,000 deaths/year in the USA [1]. Although TCCs (urothelial carcinomas) represent the majority (~90–95%) of the bladder tumours in the USA, bladder cancer encompasses a wide spectrum of malignancies, including squamous cell carcinoma (SCC; 2–5%), adenocarcinoma (0.5–2%), small cell carcinoma (<1%), and other less common histologies. Owing to its higher incidence, TCC has historically received the most research attention, whilst other histopathological types including SCC have been understudied.

SCC is divided into two subtypes, SCC associated with bilharzia infection (schistosomiasis), i.e. bilharzial-associated SCC (B-SCC) and SCC not associated with bilharziasis, i.e. non-bilharzial-associated SCC (NB-SCC). B-SCC and NB-SCC differ in their epidemiology, natural history, and clinicopathological features [2] (Table 1). B-SCC is predominantly found in regions where schistosomiasis is endemic, such as in the Middle

East, Southeast Asia, and South America [3]. In the USA, NB-SCC has been reported in patients with spinal cord injury (SCI), particularly following long-term use of an indwelling catheter [4–6]. Patients with NB-SCC are generally diagnosed at a late stage and present with poor prognosis [3]. Both B-SCC and NB-SCC are treated with radical cystectomy (RC); the use of other treatments, including neoadjuvant and adjuvant therapies in conjunction with RC, is not well established. We summarise below the current understanding of the epidemiology and clinicopathological characteristics of SCC and systematically review management strategies for SCC, with a focus on NB-SCC.

Methods

A search of the PubMed and Embase databases was performed using search terms ‘squamous cell carcinoma’ AND ‘urinary bladder’ AND ‘treatment’ AND (‘cystectomy’ OR ‘radiotherapy’ OR ‘chemotherapy’ OR ‘immunotherapy’). The search, which was conducted in February 2016, included all English language publica-

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