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Seminars article

Recommendations for follow-up of muscle-invasive bladder cancer patients: A consensus by the international bladder cancer network

Tahlita C.M. Zuiverloon, MSc, MD, PhD[a,b], Kim E.M. van Kessel, MD[c], Trinity J. Bivalacqua, MD, PhD[d], Joost L. Boormans, MD, PhD[a], Thorsten H. Ecke, MD[e], Petros D. Grivas, MD, PhD[f], Anne E. Kiltie, MA, DM, DSc[g], Fredrik Liedberg, MD[h,i], Andrea Necchi, MD[j], Bas W. van Rhijn, MD, PhD[k], Florian Roghmann, MD[l], Marta Sanchez-Carbayo, MD, PhD[m], Bernd J. Schmitz-Dräger, MD, PhD[n], Felix Wezel, MD[o], Ashish M. Kamat, MD, MBBS[p,*]

[a] *Department of Urology, Erasmus MC Cancer Institute, Erasmus MC, Rotterdam, The Netherlands*
[b] *University of Colorado Comprehensive Cancer Center, Aurora, CO*
[c] *Department of Pathology, Erasmus MC Cancer Institute, Erasmus MC, Rotterdam, The Netherlands*
[d] *Department of Urology, The James Buchanan Brady Urological Institute, Johns Hopkins School of Medicine, Baltimore, MA*
[e] *Department of Urology, HELIOS Hospital, Bad Saarow, Germany*
[f] *Department of Hematology/Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH*
[g] *Department of Oncology, University of Oxford, Oxford, UK*
[h] *Department of Urology, Skåne University Hospital, Lund, Sweden*
[i] *Department of Translational Medicine, Lund University, Malmö, Sweden*
[j] *Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*
[k] *Division of Surgical Oncology (Urology), Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, The Netherlands*
[l] *Department of Urology, Ruhr-University, Bochum, Germany*
[m] *Lucio Lascaray Research Center, University of the Basque Country, Vitoria-Gasteiz, Spain*
[n] *Department of Urology, Friedrich-Alexander University, Erlangen and Urologie24, Nuremberg, Germany*
[o] *Department of Urology, Ulm University Hospital, Ulm, Germany*
[p] *Department of Urology, University of Texas MD Anderson Cancer Center, Houston, TX*

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Abstract

Rationale: Several guidelines exist that address treatment of patients with nonmetastatic muscle-invasive bladder cancer (MIBC). However, most only briefly mention follow-up strategies for patients and hence the treating physician is often left to infer on what the preferred follow-up schema would be for an individual patient. Herein, we aim to synthesize recommendations for follow-up of patients with MIBC for easy reference.

Methods: A multidisciplinary MIBC expert panel from the International Bladder Cancer Network was assembled to critically assess currently available major guidelines on surveillance of MIBC patients. Recommendations for follow-up were extracted and critically evaluated. Important considerations for guideline assessment included both aspects of oncological and functional follow-up—frequency of visits, the use of different imaging modalities, the role of cytology and molecular markers, and the duration of follow-up.

Outcome: An International Bladder Cancer Network expert consensus recommendation was constructed for the follow-up of patients with MIBC based on the currently available evidence-based data. © 2018 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Disease management; Follow-up; Guidelines; Muscle invasive

* Corresponding author.
E-mail address: akamat@mdanderson.org (A.M. Kamat).

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Introduction

Bladder cancer (BC) accounts for approximately 430,000 new cases and 165,000 deaths each year worldwide. At primary diagnosis, 30% of patients have muscle-invasive disease (MIBC) and 10%−15% of patients with non-MIBC (NMIBC) will progress to muscle-invasive disease [1–3]. Depending on clinical and pathological characteristics, the standard treatment for nonmetastatic MIBC consists of neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy (RC) and pelvic lymph node dissection (PLND). Bladder sparing treatment options include optimal transurethral resection of the tumor followed by either concurrent chemoradiation (trimodality treatment) or external beam radiotherapy for patients unsuitable for chemotherapy. Despite extensive treatment with curative intent, the 5-year overall survival (OS) does not exceed 60% depending on the pathologic stage and nodal involvement [4]. Most patients recur during the first 2 years (>80%) after being treated with curative intent [5]. In case of recurrent disease, outcomes are poor due both to the aggressive nature of the tumor and the limited number of available treatment options; median OS times of patients with distant recurrence are in the range of 14 to 15 months [5–7]. Several large retrospective series of surgically treated patients with MIBC showed an increased survival in patients treated for asymptomatic recurrences versus patients treated for symptomatic recurrences, suggesting a preference for early detection [5,7].

Although various guidelines are available on treatment of MIBC, most of them only briefly mention follow-up strategies for patients and a consensus on the optimal follow-up protocol is currently lacking. Thus, the treating physician is often left to interpret what the preferred follow-up schema would be for an individual patient.

Here, the International Bladder Cancer Network (IBCN) aimed to analyze and critically assess the current major guidelines on patients with MIBC and to provide a comprehensive overview and recommendations for surveillance of these patients.

Guideline assessment

The IBCN is an independent active platform of international BC scientists and physicians, including urologists, pathologists, radiologists, medical oncologists, and radiation oncologists. From this group, members were selected to serve on the review panel for this article. All currently available guidelines on MIBC were retrieved by searching PubMed, Google, and Google Scholar databases. The search yielded 14 guidelines with a section on follow-up and these were included for assessment (Table 1) [8–18]. Important considerations for the assessment of the follow-up strategies included aspects of oncological and functional follow-up, probability and location of recurrences, frequency of visits, the use of different imaging modalities including cystoscopy, the role of cytology and molecular markers, and the duration of follow-up. Data on different follow-up schedules was extracted and statements for consensus were prepared. Finally, consensus statements were reviewed by all authors and accepted if endorsed by >75% of the authors.

Considerations regarding the follow-up of patients treated for MIBC

After treatment with curative intent, patients are monitored for early detection of recurrences, which offers the possibility to provide salvage treatment or to improve outcome in asymptomatic metastatic patients. Two main aspects should be considered in follow-up schedules: (1) oncological BC surveillance for early detection of recurrences and (2) functional follow-up after urinary diversion to detect early and late complications.

Oncological follow-up: Timing and site of recurrence

Local recurrences following RC occur in the pelvis: at the original bladder resection site or in the area of the PLND. The incidence of local recurrences following RC varies between 5% and 15% [19]. Although most recurrences manifest during the first 24 months, late recurrences can occur even up to 5 years or more after RC. Predictors of local recurrence include, pathological stage (8%−32%), nodal involvement (12%−29%), extent of PLND (6%−30%), positive surgical margins (7%−68%), and the use of perioperative chemotherapy [19,20]. Patients with local recurrence have limited salvage treatment options and, depending on tumor extent and symptoms, their management should be individualized—radiotherapy, systemic therapy and surgery, either alone or combined. Treatment is mostly of palliative intent with a median overall survival of 4 to 8 months [7,21].

Distant recurrences are found more frequently than local recurrences with an incidence of up to 50% following RC. Most likely sites are LNs, lungs, liver, and bone [22,23]. The highest frequency of distant recurrences (80%−90%) is seen within 3 years following primary treatment and most will manifest in the first 2 years [5,21]. Predictors of distant recurrence are pathological stage (pT3/4; range: 32%−62%), and LN involvement (range: 52%–70%) [24]. The reported frequency of isolated distant recurrence is 12.5% (range: 5.0%–33.8%) [20,25–28]. Treatment options are limited and include surgery in case of oligometastatic disease, chemotherapy and recently FDA approved immunotherapy [29–36].

After primary treatment, upper tract urothelial carcinoma (UTUC) occurs in 1.8% to 6.0% and represents the most common site of late recurrence (i.e., 3-year disease-free survival following RC). Tran et al. [37] showed that the cumulative incidence of UTUC in patients with MIBC is 4% at 3 years, and 7% at 5 years, maintaining a similar incidence later. In case of UTUC recurrence, the median OS is 10 to 55 months, and 60% to 67% of patients die of

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