

How to assess and improve health-related quality of life in bladder cancer patients

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Introduction

Bladder cancer (BCa) is the second most common genitourinary cancer in men and the most common in women. Every year, worldwide, more than 400,000 patients receive a BCa diagnosis and 145,000 succumb to it. Due to its high incidence and its relatively low mortality rates, especially regarding low-risk non-muscle invasive bladder cancers (NMIBC), its worldwide prevalence is estimated to reach the impressive quote of 2,677,500 patients (1). Moreover, with the aging of population, BCa will become even more frequent and develop in an even bigger public health burden (2).

This reflects into two major challenges not only for the urologist, but also for general practitioners, medical and radiation oncologists and for health care providers and policymakers. First, to improve the cost-effectiveness and management of BCa to allow affordable care for all patients; second, to provide them a satisfactory health-related quality of life (HRQOL) in every stage of the disease, from NMIBC to metastatic cancer and to the end-of-life stages. Several retrospective studies with the attempt to evaluate HRQOL in BCa patients and its modifications in relation to treatment have been conducted. Most of them had methodological limitations related to the retrospective design, the small sample-size, insufficient follow-up and lack of pre-diagnosis data (3). Recently, Smith *et al.* (4) prospectively reported the changes in HRQOL of patients receiving a diagnosis of BCa. Data were extracted from

Centers for Medicare and Medicaid Services' Medicare Health Outcomes Survey (MHOS) and Surveillance, Epidemiology and End Results (SEER) cancer registries; patients who received a BCa diagnosis within the period of interest [1998–2011] were enrolled in the study and matched with patients who did not. Patients participating in MHOS program self-reported data about HRQOL by answering two different questionnaires, based on the year of enrollment: the Medical Outcomes Study 36-item short-form health survey (SF-36) and the Veterans RAND-12 (VR-12). Both instruments aim to evaluate different aspects of HRQOL such as general health, physical functioning and vitality, social and emotional functioning and mental health.

After diagnosis, BCa patients experienced a decline in physical, mental and social HRQOL domains compared to controls. As expected, patients undergoing radical cystectomy reported the highest decline in all HRQOL domains. However, even if more evident in MIBC diseases, these changes were observed in all patients receiving a BCa diagnosis, regardless from the stage. Finally, the authors tried to identify possible predictors of higher HRQOL decline and found that the occurrence of a recent diagnosis of depression was independently associated with an impaired physical and mental HRQOL.

This is one of the first prospective population-based studies aiming to evaluate the impact of BCa diagnosis on HRQOL by comparing BCa to non-BCa patients. By confirming that BCa has a significant impact on patients'

HRQOL, independently from the stage of disease, this paper renews the interest in a field that represents a cornerstone of the doctor-patient relationship and of the decision-making process and that has been, especially from the urologic community, for too long ignored. At the same time it can be considered a question-generating paper. Actually, several points remain unsolved and need to be addressed: which is the best and the more standardized method to evaluate HRQOL in BCa patients? Which are the main causes of HRQOL impairment in NMI and MIBC patients? How could this impairment be reduced in the next future?

Assessment of quality of life in BCa patients

HRQOL assessment should take into account physical, emotional, social and functional domains. Usually, the assessment is conducted using generic and disease-specific validated instruments. Many tools have been used to assess HRQOL in BCa patients and they include general instruments, which usually address problems ranging from physical functioning to mental health to pain, and BCa specific instruments. In US the most widely accepted BCa specific instruments are the Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index (FACT-VCI) and the Bladder Cancer Index (BCI) (5). To date, these are the only two available validated instruments with psychometric measures. Other two tools (EORTC-QLQ-NMIBC24 and QLQ-BLM30) have been developed and are currently undergoing validation through the EORTC clinical trials.

However, each of these instruments varies in its development, validation and applicability to certain disease states. Therefore, the choice of the right instrument for the right patient remains, to date, a matter of debate. Danna *et al.* proposed a decision tree for instrument selection: in case of NMIBC investigators should use the non-validated NMIBC24 while, in case of MIBC, either the non-validated BLM-30 or the FACT-VCI. The BCI should be administered for comparison across disease stages and treatment modalities.

Quality of life in non-muscle invasive BCa patients and future perspectives

NMIBC represent approximately 75% of new diagnosed BCa (6). Nevertheless, most of the literature about HRQOL in BCa focused on patients with invasive disease

undergoing radical cystectomy and urinary diversion; the evaluation of HRQOL in NMIBC patients remains a poor investigated topic. However, few previous publications agreed in showing a relevant HRQOL decline after NMIBC diagnosis (7) and after intravesical treatment (8).

Actually, it has to be taken into account that, even if patients with NMIBC have a relatively favorable prognosis, with a 10-year cancer-specific survival (CSS) of 75–80% in high-grade and almost 100% in low-grade NMIBC (9), the majority of them will experience intravesical disease recurrence and a non-negligible percentage will develop muscle-invasive disease (10). Therefore, in these patients, intravesical treatments aiming to increase the recurrence and progression-free survivals as well as an intensive follow-up are required. The latter generally consists of regular surveillance cystoscopy and voided urine cytology with periodic upper urinary tract imaging (11). The intensity and invasiveness of these tests can lead to a non-negligible morbidity and compromise patients' HRQOL, despite of the gravity of the disease.

The advent of urinary biomarkers in NMIBC setting could theoretically obviate the need of invasive testing or at least reduce its frequency by detecting disease recurrence before it becomes clinically evident or by excluding its presence. To date, the unsatisfactory performance of the majority of urinary biomarkers approved for NMIBC surveillance has limited their clinical value. However, a new generation of promising biomarkers is currently under investigation and it is likely that, in the next future, they will enter in clinical practice, thus radically changing the follow-up scheme of BCa patients with a consistent impact on the financial burden of BCa and on patients' HRQOL.

Quality of life in muscle-invasive BCa patients and future perspectives

The HRQOL decrease in patients with MIBC is mainly related to the morbidity of radical cystectomy and to the adverse events linked to systemic therapies in the advanced and metastatic setting. The impact of radical cystectomy is mainly due to the related urinary diversion. Several studies tried to compare the different impact on HRQOL of different diversion after surgery, with contrasting findings. A recent published meta-analysis of retrospective non-randomized studies reported an advantage for ileal orthotopic neobladder compared to ileal conduit in maintaining a satisfactory HRQOL level (12). On the other hand, ileal conduit seems to allow better urinary and

sexual functions compared to orthotopic neobladder, at the cost of a dramatic change in the self-perceived body image. Probably, a definitive conclusion will not be reached since too many factors such as age, sex, social, physical and mental status can influence the outcome of a specific urinary diversion and should be taken into consideration in the decision-making process. Nevertheless, it has to be underlined that, independently from the urinary diversion performed, patients undergoing radical cystectomy experience significant declines in multiple components of physical and mental HRQOL compared to non-cancer controls, and similar to those of patients with colorectal cancer (13). Independently from the surgical approach (open, laparoscopic or robot-assisted), radical cystectomy remains a high morbid procedure and this should always be discussed with patients in the decision-making process (14).

The second factor that impacts on the HRQOL in MIBC patients concerns the toxicity related to the administration of systemic chemotherapy. Actually, cisplatin-based chemotherapy is known for its nephrotoxicity, ototoxicity and emesis. However, a breakthrough could be represented by the recent advent of immunotherapeutic agents. Their improved tolerability over chemotherapy, mainly due to their targeted mechanism of action (15), promises to radically change the future of advanced disease patients, leading to a critical improvement of oncological outcomes while preserving safety and an acceptable quality of life over long periods of cancer cycle.

Conclusions

While some studies have addressed HRQOL in BCa, several gaps remain to be filled for this context in such a complex disease in terms of variability in pathology, prognosis and treatment modality.

Future efforts in this respect should concentrate to identify the most appropriate psychometric tools worthy to be tested prospectively and to be entered in routine clinical practice.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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