Author’s response to reviews

Title: Unmet needs in sexual health in bladder cancer patients: A systematic review of the evidence

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Author’s response to reviews:

Dear editor(s),

We thank the reviewers for taking the time to review the manuscript and for their valuable comments. Please find their comments and our replies below. The manuscript has been uploaded separately with tracked changes.

All co-authors have reviewed and approved the revised manuscript. We hope that the reviewers now find the manuscript more suitable for submission.

Many thanks,

Agustina Bessa, on behalf of all co-authors

Reviewer 1:

The idea of the paper is good but as the authors wrote there is no enough quality study on the topic.
Thus, authors should build the discussion section on indirect relationship between quality of life of BC patients with their sexual life.
Additionally, papers on penile prosthesis after cystectomy can be added.

Response:
Thank you for this comment. We agree with the reviewer and have consequently added more discussion on the relationship between sexual wellbeing and health-related quality of life. We have discussed how the aspects of sexual wellbeing are measured in the context of health-related quality of life from a questionnaire perspective, whilst also looking at individual targets and social context (Discussion, page 8-9). Regarding penile prosthesis, although we understand the importance of this treatment for erectile dysfunction, we believe the focus of the discussion should be on the impact of sexual wellbeing and quality of life in a general way for both men and women and on the challenges of how it is measured. The following paragraph was added to the discussion: Moreover, our systematic review highlights how sexual health may negatively impact on mental wellbeing and HRQoL – and hence indicates the need to address this gap for patients. As suggested by the definition of the WHO [4], sexual health has to be evaluated from a psychosocial perspective and not only the physical and physiological aspects. Although erectile dysfunction in men and physical and physiologic changes associated with cystectomy in women are the dominant factor driving sexual function, other causes of sexual dysfunction, such as depression or anxiety related to changed body image, distress regarding partner reaction to an altered body as well as the degree of problems that patients are experiencing due to their sexual function (bother), should be evaluated and managed.
Currently, HRQOL questionnaires like the Functional Assessment of Cancer Therapy – Bladder Cancer (FACT-BC) do include questions about interest in sex, while the Bladder Cancer Index (BCI) also includes questions about desire, arousal, sensation, and orgasm. Several EORTC questionnaires include a limited number of sexual functioning items. However, there is no single self-reported measure that covers the entire range of sexual health. Recently, the European Organization on Research and Treatment of Cancer (EORTC) developed an EORTC Sexual Health Questionnaire (EORTC SHQ-22) for assessing sexual health in cancer patients [27]. In addition to that, HRQOL assessment should target patient’s current or very recent HRQOL status. This is of interest as (1) it has been suggested that patients overestimate their baseline HRQOL in the sexual function domains by 27% [28]; and (2) it would allow to better understand the degree of problems experienced by patients (measuring “bother”). It is also important to note that function and bother do not necessarily correlate as demonstrated by Letwin et al [29] and that despite sexual health issues being an important concern to patients, they often experience difficulties in disclosing their complaints with health care providers or their partners. Lastly, as sexual wellbeing is closely correlated with social interactions, patients’ relationship status should also be considered when evaluating sexual wellbeing and its impact on HRQOL.

Reviewer 2:

Authors present an interesting study on sexual health on bladder cancer.
The topic is of interest and the study is well written.
Unfortunately, in my opinion there is an important bias in the study design: conservative treatment (transurethral resection of bladder tumor, TUR-B) is completely different from radical cystectomy. In the latter case, there is an anatomical damage to neurovascular bundle, which is not involved in TURBT. Thus, we have to distinguish between "emotional" and "anatomical" reasons affecting sexual life.
The Authors mat consider to completely split their study in two arms: TURB vs. cystectomy.

Response:
Thank you for this comment. We agree with the reviewer regarding the different impact that TURBT and cystectomy treatments can cause on sexual wellbeing of patients; it would be very interesting to provide a full review and highlight those differences if more information on TURBT was available; the majority of studies that match our inclusion and exclusion criteria are on cystectomy and therefore not enough data is available to completely split the study in two arms. We have addressed this limitation now more clearly in the discussion section: In our systematic review, most studies addressed sexual health in patients with MIBC who underwent radical cystectomy and only four studies focused on patients with NMIBC. This is potentially affecting the generalisibility of our observations as it is important to note that treatments for NMIBC and MIBC substantially differ, e.g. TURBT vs cystectomy. In a prospective study by Yoshimura et al. [31] on the impact of TURBT on QoL in patients with NMIBC, physical problems were found with the first TURBT, but when the fourth TURBT was performed, patients appeared to have adapted to frequent operations, although their general QoL remained affected. For cystectomy patients, it has been shown that although relationships with friends were unchanged, relationships with spouse or partner were disturbed by sexual problems [30]. Partner response to the presence of an external appliance, such as stoma, may also strain intimate
relationships and contribute to a dysfunctional sex life. Nevertheless, these observations highlight that 1) the threat of recurrence, multiple cystoscopies, TURBT, and intravesical instillations make QoL assessment in superficial bladder cancer challenging; 2) the importance of looking at sexual function in patients with bladder cancer in a broader way is needed, i.e. including both the physical perspective as well as the patients’ partner and relationships.