Editorial

The need to improve TURB: a diagnostic and therapeutic fundamental first step in the disease's management

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Urinary bladder cancer (BCa) accounts for about 7% of all new cancers in the USA with 81,190 estimated new cases and 17,240 deaths in 2018 (1). Approximately 75% of the new diagnoses BCa will be non-muscle-invasive BCa (NMIBC) (2) affected by disease recurrence and progression rates of approximately 60% and 20%, respectively (3). In every new diagnosed BCa, transurethral resection of the bladder (TURB) represents a fundamental diagnostic/staging tool and the gold standard treatment followed with adjuvant intravesical chemo- or immunotherapy for NMIBC (2). A well performed TURB is pivotal in the diagnostic and therapeutic processes, since it has been confirmed that the absence of detrusor muscle in the specimen is associated with a significant increased risk of residual disease, disease recurrence and tumor understaging (4).

Several surgical and technical aspects need to be highlighted for the correct disease management. The main goal of a well-executed TURB is to complete the resection, a goal that can be achieved either with *en-bloc* or fractioned resection (5). The advantage of the resection in fraction is to separate the exophytic part of the tumor and to provide enough information regarding the vertical and the horizontal extent of the tumor. On the other hand, an *en-bloc* technique can be feasible in exophytic tumors and provide a high quality of the specimen resected (5). Both techniques are feasible and depend mainly on the characteristics of the tumor and on the experience of the surgeon. Similarly, both monopolar and bipolar resection techniques are validated, whereas there is a controversy on which one is the most effective device (6).

Recently, the widespread of new methods of tumor visualization such as photodynamic diagnosis (PDD) and narrow band imaging (NBI) represent a useful tool for urologists. These techniques have shown excellent results in reducing disease recurrence rates and seem particularly effective in the detection of carcinoma in situ. However, with time their effect on reducing disease progression and cancer-specific mortality have to be proved (7). Another decisive diagnostic and therapeutic step is represented by the second look TURB to diagnose and if possible remove residual tumor in high-risk NMIBC (8). Residual tumor was found in 17–67% of patients in a recently metanalyses analyzing 8,409 patients affected by high risk NMIBC (8).

Several parameters permit to stratify risk of disease recurrence and progression of patients. Substaging groups classification have been proposed by EORTC (9) and CUETO (10) to predict outcomes and optimize treatments of NMIBC. These models include pathological features at TURB such as: number of tumors, tumor diameter, recurrence rate, T stage, grading and presence of concomitant carcinoma in situ. However, other elements need to be considered by urologists to individualize the best therapeutic options, such as: gender, smoking status and presence of histological variants. The impact of gender on pathological features and outcomes have been examined demonstrating a reduced risk of developing BCa in females even though female patients that have developed BCa show worse disease recurrence and progression rates (11). Smoking status is a well-known risk factor for the BCa development but has also an important role in defining

recurrence and progression rate. Urologists should counsel active smoker diagnosed with BCa to quit smoking habits as an active part of the therapeutic management (12). Finally, histological variants at TURB, although affected by poor concordance rate compared to RC (13) have to be considered in the therapeutic management of BCa and should be considered before deciding to opt for either a conservative or a more aggressive strategy (14).

Regarding the approach after a well performed TURB, the use of a single instillation of chemotherapy should be recommended in all patients harboring low- or intermediate-risk NMIBC. The instillation should be delivered within 24 hours and epirubicin or mitomycin as well as gemcitabine seem effective in reducing recurrence rates (although no evidence exists with regards to disease progression) (15,16). In case of perforation, extensive resection or persistent hematuria, the single instillation should be avoided due to the risk of incurring in severe complications. On the other hand, not all the tumors need to be treated since some selected cases might be controlled with active surveillance (17).

Finally, another important question is when to opt for an early cystectomy since patients progressing into a muscle-invasive disease after a prior history of NMIBC have been shown to have worse survival outcomes than those *de novo* muscle-invasive bladder cancer (18). New markers are needed to understand which tumors harbor the most adverse prognoses and therefore might need an aggressive disease management. Although the therapy with BCG composed by induction and maintenance for intermediate and high-risk NMIBC is effective with a level of evidence 1a in reducing disease recurrence and progression, new device assisted intravesical chemotherapy has been proposed and might find a role in the treatment of patients who failed BCG and decline RC (2,19). Furthermore, clinical trials are evaluating the emerging role of immune check point inhibitors also in the NMIBC setting. Considering the follow up schemes of NMIBC patients, data are urgently requested to understand the correct timing of CT-scan, cystoscopy and cytology as most of the data are based on historical retrospective series. Moreover, emergent non-invasive biomarkers have been proposed but none has reached daily practice in order to replace the more invasive but gold standard cystoscopy (20).

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Footnote

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

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