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LETTER TO EDITOR

Office-based management of Non-Muscle Invasive Bladder Cancer (NMIBC): A position paper on current state of the art and future perspectives

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To the Editor,

Bladder cancer is one of the most common cancers in humans, representing the 7th and 17th type of neoplasm in both genders (1). Its incidence and mortality are quite heterogeneous in different countries and are due to different risk factors, quality and prevalence of healthcare and the possibility of early diagnosis and treatment of the tumor and its potential recurrences (2-3). Bladder cancer can be divided into *muscle-invasive* (MIBC) and *non-muscle invasive* (NMIBC). Early detection of the primary tumors and the recurrences is of paramount importance to enable a better prognosis (3).
While MIBC is known to be treated very aggressively, i.e. with surgery, radiotherapy, and chemotherapy (4-8), NMIBC has a better prognosis but still has a high recurrence rate despite measures such as the use of local drugs. Although most of these recurrences in low-grade tumors guarantee a good prognosis if treated promptly with TURB, they still pose a management problem for both the patient and the healthcare system.
Indeed, the patient is often forced to undergo multiple anesthesia, surgical and psychophysical stress related to hospitalization and the anxiety of the operation itself. Furthermore, performing a *transurethral resection of the bladder* (TURB) may lead to transport management issues and organization problems for the patient's family. From a healthcare perspective, hospitalization for TURB requires an economic cost of several thousand euros, considering the cost of the surgical staff, the materials used during the operation and the hospital stay (9, 10). Furthermore, this contributes to longer waiting lists, which also has a negative impact on other patients. This problem is highly relevant, given the organizational problems of healthcare systems and surgical waiting lists in the post-COVID era (11).
Last but not least, there is the "*green*" problem considering that further hospitalization requires more surgical and hospital supplies, an increase in travel for patients and relatives, and thus an impact on the carbon footprint.
The EAU guidelines also include office-based fulguration and laser vaporization among the possible treatment options for NMIBC (3). Specifically, it states that that patients with a history of small Ta LG/G1 lesions can undergo fulguration or laser vaporization on an outpatient basis for small papillary recurrences.
Outpatient treatment can be performed either by fulguration or using laser, generally under local anesthesia with instillation of intravesical lidocaine prior to the procedure and may warrant histologic examination by pre-fulguration biopsy. If HG is found, the patient can then be scheduled for TURB in the following weeks.
The literature now presents numerous reports on the efficacy and safety of performing office-based procedures for the treatment of NMIBC (12-19). Recently, *Vitug et al.* evaluated the outcomes of fulguration in 270 patients with recurrent TaLG NMIBC in an outpatient setting (20). The 10-year incidence of *cancer-specific mortality* (CSM) and progression were

0% and 3.1%, respectively. They estimated a savings of nearly 7,000 Canadian dollars per patient. The savings in economic terms have also been demonstrated by other authors in other contexts (15, 21-23).
Pedersen et al. in a prospective randomized controlled trial proved that laser photocoagulation in an outpatient setting is non-inferior to standard TURB for the 4-month recurrence rate (24).
Halstuch et al. introduced an additional step, namely the use of a single dose of mitomycin (MMC), after performing office-based procedures such as fulguration (25). They found that a single dose of MMC instilled after fulguration was associated with longer recurrence free survival (RFS) compared to patients who did not receive MMC after the procedure, with no high-grade complications.
One of the potential limitations of office-based procedures is the pain experienced by the patient. However, *Strock et al.* evaluated the pain perceived by patients during the procedure and obtained satisfactory results in this respect. The VAS scores after diagnostic cystoscopy report no or only mild pain in the totality of their case series.
Despite the current evidence, we are still far from knowing which patients are safe candidates for these procedures (number of lesions, size of lesions, number of previous TURB with histologic pTa LG/G1, age, etc.) and to consider these procedures the "*standard of care*" in selected patients.
We believe that outpatient treatment of NMIBC should be implemented for reasons of economic and environmental sustainability as well as for reasons of benefit to the patient, as illustrated previously. A stronger stance in national and international guidelines in favor of these procedures in selected patients could be of fundamental importance. However, for the committees to move further in this direction, the scientific community must bring results from further randomized trials, perhaps multicenter, which can make the scientific evidence stronger.
Furthermore, the definition of the ideal candidate for these procedures is un unmet need. Since it is now clear that that the patients for whom the treatments are indicated are patients with relapses of a previous pTa LG/G1 in the absence of rare variants of bladder cancer, some inclusion criteria need to be defined more precisely such as age, number of recurrences/papillary lesions, time since the last TURB, etc.
In this sense, the application of new biomarkers could become useful to define the patients with the highest risk and therefore not subject them to office-based treatment.
Furthermore, the definition of the patient eligible for these procedures is also fundamental. It has now been established that the patients for whom the treatments are indicated are patients with relapses of previous pTa LG/G1 in the absence of rare variants of bladder cancer, some inclusion criteria must be defined in more detail such as age, the number of relapses/papillary lesions, time since last TURB, etc.
In this sense, the application of new biomarkers could become useful to define the patients most at risk and therefore not candidate to office-based treatment (26).
In conclusion, we believe that the office-based management of NMIBC should be much more under the spotlight of the scientific community. It is essential to properly define either the ideal candidates and the optimal settings.

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