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Optimized management in patients with bladder cancer

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There is no doubt that surgical treatment, including both transurethral and radical procedures, remains the critical step in the management of patients with bladder cancer. This is particularly true even now, many decades after the introduction of current management principles.

We all feel however, that only small improvement in treatment results can be demonstrated during the last few years. The most important reason is lack of really effective systemic or local medical therapies, but to some extent also our inability to provide critical and scientifically correct evaluation of some crucial treatment steps.

Authors of the paper [1] should be congratulated for their thorough analysis of cystectomy performance in different European urological departments. Even after this report, however, there remain several questions which need to be answered. Moreover, scientifically correct answers must be incorporated in the daily practice of patients´ care management.

I fully agree with the authors, that cystectomy delay is connected with the risk of tumor upstaging and of treatment failure. Apparently and logically, optimal results can be achieved when surgery is performed at the time of bladder confined disease. As we have no imaging modality which could reliably detect the extent of disease, neither at the time of transurethral resection of bladder tumor (TURB) nor at the time of cystectomy, we use surrogate parameters to demonstrate the optimal timing of surgery.

One of these parameters is the interval between the last TURB and cystectomy. There was demonstrated by several authors, that the interval over 3 months is connected with advanced pathological stage (ref. 11, 12 of the article), disease – specific (ref. 8, 9 of the article) and overall survival (ref. 8, 9, 12 of the article). These results, however, need to be evaluated with caution. They are based on retrospective series, some of them on data reported from databases. They cannot provide all the necessary information important for evaluation of all potential aspects which can influence treatment delay. There are therefore many confounders which can bias the final conclusions. It is no surprise that some groups recommend the shorter interval than 3 months necessary for optimal results [2] and some, in the contrary, report no negative influence of treatment delay [3].

There is even less information available for patients with clinical non-muscle invasive bladder cancer indicated for cystectomy. We know from retrospective series that waiting for muscle invasive progression is connected with worse oncological outcomes [4], but to my knowledge, the precise interval between diagnosis of non-muscle invasive BCG failure and cystectomy has never been demonstrated.

The incorporation of neoadjuvant systemic chemotherapy in muscle invasive tumors modify time schedules significantly. Although not reported by authors of the article, it is connected with the extended interval between TURB and radical cystectomy. The recommendation for universal indication of neoadjuvant chemotherapy makes considerations even more complicated, as we do not know which individual cases will respond and profit and which will progress because of the postponement of surgery.

Which recommendations can be applied in daily practice with respect to this information?

We know that the earlier we perform cystectomy after TURB the lower the risk of treatment failure can be expected. For this reason, we must adapt the organization of care accordingly:

1. As the majority of data confirm the beneficial role of the 3 month interval, it should be used as a rule and incorporated in algorithms and recommendations.
2. But our routine practice must be much more flexible. I am deeply persuaded, that the approach can

be individual even with the current level of knowledge. There are apparently cases where a 3 month interval is too long, like with aggressive undifferentiated tumors, tumors with adverse pathologies or rapidly progressing tumors after history of non-muscle invasive disease. Additionally, we must respect individual clinical situations like bleeding, hydronephrosis, etc.

3. As neoadjuvant chemotherapy is recommended by guidelines it should be considered in all cases, particularly with extravesical extension. The close cooperation with medical oncologists is necessary to prevent delay before and after chemotherapy.
4. The whole system of care should work very effectively by including a flexible waiting lists for different diagnostic procedures, by cooperation between referral centers and outpatient urologists or smaller departments as transition between hospitals can cause treatment delay [5], etc.
5. Public and general practitioners should be informed about the symptoms of bladder cancer to prevent hesitation in visiting a urologist.
6. We must keep in mind that urologists are responsible for bladder cancer management, including organization of care and information for public.

But real breakthrough in the quality of care will be based on future achievements:

1. We must have more precise imaging modalities and prognostic factors to be able to specify exactly the extent and predict the aggressiveness of the disease at any moment during management. This knowledge will help us to make the indication of radical cystectomy in time and in those patients who will really profit from radical approach.
2. We must understand tumor biology to be able to provide precise and individual indication of neoadjuvant chemotherapy. Moreover, we urgently need more effective systemic therapy with less morbidity.
3. We must understand exactly all the consequences of aggressive TURB. Recently published observations of the risk of systemic cancer cell seeding during TURB for muscle invasive bladder cancer [6] can have several consequences and possible implications in clinical practice. If it were confirmed by further studies and if it were connected with tumor progression, we would have to reconsider the strategy of TURB in apparently muscle invasive tumors, its timing and combination with systematic chemotherapy.

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