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The arguments for an early cystectomy in patients with urothelial carcinoma

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At the initial diagnosis of bladder cancer, 70% of cases are diagnosed as non–muscle–invasive bladder cancer (NMIBC) and approximately 30% as muscle–invasive bladder cancer (MIBC).

Among patients treated with radical cystectomy due to MIBC, 57% had muscle invasion at presentation, while 43% were initially diagnosed with NMIBC which had progressed, despite organ–preserving treatment. Approximately one–third of patients diagnosed with MIBC have undetected metastases at the time of treatment of the primary tumor, while 25% of patients who undergo radical cystectomy present with lymph node involvement at the time of surgery. In cases of MIBC, a cystectomy should not be delayed for >3 months because this delay can increase the risk of progression and cancer–specific mortality (Grade B, EAU Guidelines) [1, 2].

One of the most challenging clinical decisions concerning bladder cancer is the treatment of pT1 high grade tumors. This tumor category is very heterogeneous and requires a special approach. According to the EORTC data, intermediate and high–risk NMIBC should be treated with BCG (*Bacillus Calmette Guerin*) instillations for at least one year. An individual recurrence and progression risk profile can be assessed using the EORTC–trial, which is composed of over 2500 patients [3]. However, only 7% of the EORTC–collective has been treated with BCG, so the progression risk is overestimated here. The challenge is to find the balance between overtreatment and understaging [4].

The response to BCG–therapy depends on the residual tumor status in TUR and on the presence of CIS. BCG–failure occurs in about 50% of cases and is defined as a relapse or progression to MIBC, a higher tumor grade, or CIS during 3 month and 6 month follow up visits. Patients with BCG failure or recurrence after BCG are unlikely to respond to further BCG therapy; therefore, radical cystectomy is the preferred option. This underlines the need to recommend early radical cystectomy, especially in case of failure of intravesical therapy. According to EAU guidelines, immediate radical cystectomy should be offered to those patients with BCG–failure and NMIBC who are at highest risk of progression [4]:

– Multiple and/or large (>3 cm) T1, high grade tumors
– T1, high grade tumors with concurrent CIS
– Recurrent T1, (HG/G3) tumors
– T1, G3 and CIS in prostatic urethra
– Micropapillary variant of urothelial carcinoma

Shariat et al. analysed the correlation between clinical (TUR specimen, imaging, bimanual examination) staging before and pathological staging after radical cystectomy. Nearly half (48%) of cT1–patients were upstaged after cystectomy [5]. One of the problems is a low objective reproducibility of the evaluation of TUR pathology. Delay of radical cystectomy may lead to decreased disease–specific survival [6]. A systematic review of over 3000 patients demonstrated the progression of pT1, from high grade to MIBC, in 21% of patients and 14% died as a result of BCa after a median follow–up of 48–123 months. These events occurred relatively early, mainly within 48 months [7]. In another trial 33.4% were upstaged to non–organ–confined stage (≥T3), 16.2% presented lymph node metastases and 35.5% of patients died of metastatic disease during the 2 year follow–up [8]. The overall oncological outcome is good in ≤pT3, pN0 stages and gets dramatically worse with positive lymph nodes and positive surgical margins. We have also learned from studies concerning neoadjuvant chemotherapy, that a delay of cystectomy of over 3 months can lead to worse pathology results and decreased survival [1].

Another argument for an early cystectomy is the functional postoperative result. An early cystectomy for T1–tumor with a possibility of orthotopic urinary diversion is a reasonable oncological treatment option for men and women. The best possible functional result, with high continence and maintained sexual function, can be achieved in these cases due

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to the preservation of neurovascular bundles in men and of lateral vaginal walls in women [9]. With increasing age there is a higher risk for comorbidities and complications after cystectomy.

Poletajew and colleagues present data on the waiting time of patients with urothelial carcinoma of the bladder from establishing the indications for radical cystectomy to surgery in Polish urological centres and analyse the factors that influence it. The waiting time in most cases in Poland did not exceed 90 days, with shortest referral times occurring in provincial hospitals (median waiting time 45 days). However, in the substantial number of cases (22%, 121 patients) radical cystectomy was postponed significantly over 90 days [2]. It would be of great value to compare the disease specific survival of the patients with the waiting time over 90 days *vs.* those with a time of less than 90 days. Further studies could help to determine the influence of cystectomy delay on functional outcome and patient survival.

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