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UROLOGICAL ONCOLOGY

Who needs numbers more: patients or doctors?

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One of the most burning problems of modern urology still remains the treatment of bladder cancer, which has the highest recurrence rate of any malignancy. Depending on a patient's individual characteristics, the probability of recurrence of non-muscle invasive bladder cancer (NMIBC) at one-year ranges from about 20% to 72% and the probability of progression at five years ranges from about 5% to 45%. In 2006, Sylvester et al. published a paper based on data from 2,596 patients with NMIBC included in seven trials conducted by European Organization for Research and Treatment of Cancer (EORTC) [1]. Their aim was to provide a simple scoring system based on universally assessed clinical pathological factors, which might allow urologists to easily calculate the risk of recurrence and progression after transurethral resection of the bladder tumor (TURBT). Many authors verified the value of this calculator whether it may be replicated and adopted into every day practice. The results were divergent, mostly due to smaller number of cases than those impressively collected by Sylvester. Altieri et al. and Fernandez-Gomez et al., after analysis of 259 and 1,062 cases of NMIBC respectively, found them useful for stratification of recurrence and progression in their cohorts, and suggested the introduction EORTC risk tables into clinical practice [2, 3]. However, a multicenter Spanish team concluded that the discriminative ability of the EORTC tables decreased in patients with BCG progression and overestimated the risk of recurrence in this subgroup of patients [3]. In other words, it makes these tables less useful in high-risk patients. The practical proposal from these and some other studies may be expressed by generally stating that patients from groups stratified as high-risk need more frequent and careful follow-up [4].

The authors of the paper published in this issue of CEJU performed another external validation of EORTC tables in the group of 91 patients with NMIBC [5]. However, this paper concerns clinically important problems, but while both the incidence of bladder cancer is high and EORTC tables still need to be validated in contemporary series of patients, in my opinion, the authors leave us with some unaddressed and unexplained issues. First of all, I feel the lack of clear definition of progression used by the authors. If it was proven by pathological examination, what was the protocol and classification used? Time to progression as defined by EORTC is the time from randomization to the date of first increase to T2 or higher stage [1]. In most of patients this results with withdrawal from further follow-up and the decision about cystectomy. On the other hand, patients with low-risk cancers would benefit from less intensive therapy and surveillance. As authors admit the poor reproducibility of pathologic stage and grade is a well and widely recognized problem. A clear definition must be established in order to standardize the results of different studies and because of the important impact of the clinical decisions about adjuvant therapy, that may be taken based on the nomograms. Even more vital for the individual patients may be the decision about abandoning a bladder preservation approach. The crucial factor, which determines the risk of recurrence, is the quality of primary performed TURBT procedure, as we know that the tumor on a reTURBT in high-risk patients is present in up to half of cases. This high quality is expressed by the most reliable oncological radicalness, personal surgical integrity, and dealing according to the most up-to date clinical and pathological protocols. All this can only be achieved by years of training in highvolume centers. As the authors stated, among other things, tumor recurrence can be attributed to a combination of missed lesions and not complete initial resection, I suppose they are appreciative of well-performed TURBT.

As the presence of CIS is considered a strong prognostic factor, both for recurrence and progression. the number of patients with accompanying presence of intraepithelial neoplasia may strongly interfere with the results obtained. In the EORTC, CUETO and UK groups the percentage of CIS-positive cases were 4.4, 7.5, and 8.3% respectively [1, 2, 6]. The authors' data are roughly the same. Ufortunately, they do not provide the information about the method of diagnosis of CIS (NBI, PDD, biopsy taken?). I would be grateful for the explanation because, in my center, the diagnosis of CIS is a bird of big rarity. Currently, prognostication of patients with all forms of bladder cancer is hampered owing to the inadequacy of clinicopathological risk factors to accurately predict individual treatment outcomes. Therefore, there is

definitely an urgent need for having reliable genetic or molecular markers of bladder cancer. There are many of them studied currently and in the past, also by the authors [7–10]. On one hand, I regret that they did not use their investigational experience to combine clinical, pathological, and molecular variables in order to identify a powerful and objective tool to be used in daily practice. On the other hand, I

References

- Sylvester RJ, van der Meijden APM, Oosterlinck W, Witjes JA, Denis L, Newling DW, Kurth K. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORT risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol. 2006; 49: 466–477.
- Altieri VM, Castellucci R, Palumbo P, Verratti V, Sut M, Olivieri M, et al. Recurrence and progression in non–muscle–invasive bladder cancer using EORTC risk tables. Eur Urol. 2012; 89: 61–66.
- Fernandez–Gomez J, Madero R, Solsona E, Unda M, Martinez–Pineirol, Ojea A, et al. The EORTC tables overestimate the risk of recurrence and progression in patients with non–muscle–invasive bladder cancer treated with Bacillus Calmette–Guerin: External Validation of the EORTC risk tables. Eur Urol. 2011; 60: 423–430.
- Bobiński J, Lipiński M: The value of EORTC risk tables in evaluating the results of patients treated for non–muscle invasive

bladder cancer with TUR. CEJU. 2009; 62: 237–242.

- Borkowska EM, Jędrzejczyk A, Marks P, Catto JMF, Kałużewski B. Predicting recurrence and progression in individual patients with non– muscle invasive bladder cancer using EORTC risk tables. CEJU. 2013; 66: 14–20.
- Pillai R, Wang D, Mayer EK, Abel P. Do standardized prognostic algorithms reflect local practice? Applications of EORTC risk tables for non-muscle invasive (pTa/pT1) bladder cancer recurrence and progression in a local cohort. Scientific World Journal. 2011; 11: 751–759.
- van Rhijn BW, Liu L, Vis AN, Bostrom PJ, Zuiverloom TC, Fleshner NE, et al. Prognostic value of molecular markers, substage and European Organisation for the Research and Treatment of Cancer risk scores in primary T1 bladder cancer. BJU Int. 2012; 110: 1169–1176.
- 8. Borkowska E, Jędrzejczyk A, Kruk A, Pietrusiński M, Traczyk M, Rożniecki M,

would be happy to congratulate the authors for creating such a tool in the future.

There is no clear answer to the question presented in the title. It seems that patients need small number of oriented and well educated urologists who might use big numbers for the their best interests at heart and mind. This is what EORTC tables were created for.

> Kałużewski B. Significance of CDKN 2A gene A148T variant in patients with bladder cancer. CEJU. 2011; 64: 168–174.

- Słojewski M, Złowocka E, Cybulski C,Górski B, Debniak T, Wokołorczyk D, et al. CHEK2 germline mutations correlate with recurrence rate in patients with superficial bladder cancer. Ann Acad Med Stetin. 2008: 54: 115–121.
- Alkhateeb SS, Neill M, Bar–Moshe S, Rhijn BU, Kakiashvili, Fleshner M, et al. Long–term prognostic value of the combination of EORTC risk group calculator and molecular markers in non–muscle–invasive bladder cancer patients treated with intravesical Bacille Calmette–Guérin. Urol Ann. 2011; 3: 119–126. ■

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