

**Editorial comment to:** Kliment J Jr, Elias B, Baluchova K, Kliment J Sr. The long-term outcomes of radical prostatectomy for very high-risk prostate cancer pT3b-T4 N0-1 on definitive histopathology. *Cent European J Urol.* 2017; 70: 13-19.

## Radical prostatectomy in locally advanced cancer – an indispensable onset of multimodal therapy?

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Prostate cancer (PCa) remains one of the most common malignancies diagnosed in males worldwide [1, 2]. Introduction of the prostate specific antigen (PSA) has revolutionized both the diagnosis and therapy of PCa. We have learned that PSA-based screening has the potential to reduce prostate cancer specific mortality, yet it is inherently linked to unacceptable rates of overdiagnosis. Therefore, to reduce treatment-related morbidity, active surveillance protocols were introduced and offered to a growing number of patients. Although, the mainstay therapy for organ-confined disease is still radical prostatectomy (RP) the role of surgery is shifting towards more advanced cases leaving low risk disease behind [3].

According to the most current European Association of Urology Guidelines, radical prostatectomy may be offered to a highly selected group of patients with locally advanced cancer in the setting of a multimodal approach, the standard of which remains to be developed on [4]. In the past, surgical treatment was reserved for organ-confined disease only.

In the current issue of *Central European Journal of Urology* Kliment et al. provided results of the study on the long-term outcomes of radical prostatectomy in high risk patients [5]. The authors analysed the cohort of patients who underwent radical prostatectomy and were diagnosed with cancer invading seminal vesicles or other adjacent structures regardless of their lymph nodes status and perioperative treatment. Survival curves of the entire cohort were introduced and confirmed favourable and decent outcomes. After 10 years 69,2% of men survived without clinical progression.

The authors have shown how heterogenic high-risk prostatic cancer might be. Patients differed significantly in terms of stage and Gleason score. Moreover, the concordance between clinical and pathological stages was not satisfactory. Even more, significant discrepancies were found between biopsy and specimen Gleason scores. These issues may hamper opti-

mal management if radiation with or without androgen deprivation is implemented up front based only on risk stratification. In the meantime, advancement of multiparametric magnetic resonance imaging (mpMRI) has been observed. Accuracy of mpMRI in proper staging reaches 85% in high risk disease [3]. Nowadays, its use is recognized as an essential tool in imaging before the commencement of therapeutic decisions, especially surgical ones.

In the study, multimodality approach involved neoadjuvant androgen deprivation therapy. Although not recommended by EAU Guidelines, almost one fifth of the patients received ADT before operation. Randomized clinical trials proved that its use in fact decreases the rate of positive surgical margins, but does not prolong survival [6, 7]. Interestingly patients with ADT as neoadjuvant therapy were at higher risk of biochemical and clinical progression when compared to those without hormonal manipulations. The cause of this phenomenon has not been fully elucidated. Theories exist that neoadjuvant ADT in fact does not reduce the incidence of PSM, but alters architecture of the specimen that obscures correct staging and grading [8]. One may further hypothesize that patients with misdiagnosed negative surgical margins may not obtain appropriate treatment.

The analysis has shown that adjuvant ADT decreases the risk of biochemical progression. A quarter of men subjected to radical prostatectomy due to locally advanced disease needed no adjuvant therapy. Taking into consideration side effects of hormone therapy, its potential avoidance in surgical approach makes a huge benefit over definitive radiotherapy (RTX) in high risk patients. Timing of administration and proper selection of patients who may benefit the most from adjuvant treatment remains of utmost importance. On the other hand reliable, prospective and at best randomised comparison of radical prostatectomy and RTX in high risk prostate cancer

remains an empty space in the uro-oncological field. To conclude, this study provides incremental evidence to suggest that radical prostatectomy is the first reasonable step and in some cases the last step in the treatment of locally advanced, high risk disease. Surgery proved to be the best staging tool. Further treatment may be offered based on 'real stage' and 'real grade' of PCa and not on suspected ones. Nowadays, the urologic community has begun to answer the question whether radical prostatecto-

my is beneficial in more advanced disease. The exciting idea of local surgery in the setting of limited bone-metastatic disease has just emerged and is based on the satisfactory results of surgical approach in patients with positive lymph nodes [9]. Recruitment to three prospective randomised trials has started and primary results are expected in the beginning of the next decade. In the light of these new groundbreaking studies, we may be witnessing the ultimate limit of surgical treatment in prostate cancer.

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