Immediate radical cystectomy versus BCG immunotherapy for T1 high-grade non-muscle-invasive squamous bladder cancer: an international multi-centre collaboration

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Abstract

Purpose To compare cancer-specific mortality (CSM) and overall mortality (OM) between immediate radical cystectomy (RC) and Bacillus Calmette–Guérin (BCG) immunotherapy for T1 squamous bladder cancer (BCa).
Methods We retrospectively analysed 188 T1 high-grade squamous BCa patients treated between 1998 and 2019 at fifteen tertiary referral centres. Median follow-up time was 36 months (interquartile range: 19–76). The cumulative incidence and Kaplan–Meier curves were applied for CSM and OM, respectively, and compared with the Pepe–Mori and log-rank tests. Multivariable Cox models, adjusted for pathological findings at initial transurethral resection of bladder (TURB) specimen, were adopted to predict tumour recurrence and tumour progression after BCG immunotherapy.

Results Immediate RC and conservative management were performed in 20% and 80% of patients, respectively. 5-year CSM and OM did not significantly differ between the two therapeutic strategies (Pepe–Mori test p = 0.052 and log-rank test p = 0.2, respectively). At multivariable Cox analyses, pure squamous cell carcinoma (SqCC) was an independent predictor of tumour progression (p = 0.04), while concomitant lympho-vascular invasion (LVI) was an independent predictor of both tumour recurrence and progression (p=0.04) after BCG. Patients with neither pure SqCC nor LVI showed a significant benefit in 3-year recurrence-free survival and progression-free survival compared to individuals with pure SqCC or LVI (60% vs. 44%, p = 0.04 and 80% vs. 68%, p = 0.004, respectively).

Conclusion BCG could represent an effective treatment for T1 squamous BCa patients with neither pure SqCC nor LVI, while immediate RC should be preferred among T1 squamous BCa patients with pure SqCC or LVI at initial TURB specimen.

Keywords CG · Immunotherapy · Immediate radical cystectomy · Non-muscle-invasive bladder cancer · T1

Comment

In the current issue of Journal Club CAU we will discuss the work published in World Journal of Urology by Dr. Chiara Lonati and collaborators with the support from European Young Academic Urologist, issue published on February this year.

Bladder cancer (BCa) is the 11th most common cancer, knowing that 75% of the previously mentioned are non-muscle-invasive [i]. We have solid evidence for urothelial bladder cancer (UBC) treatment. Nevertheless, the histological variants present difficulties in correct treatment course owed to the minimum clinical trials showing sufficient evidence regarding this pathology.

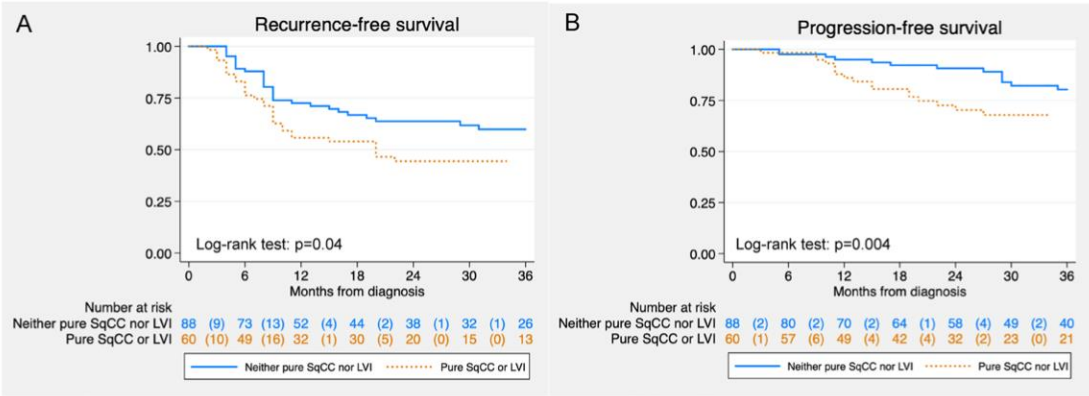
Standard treatment for stage T1 is based on transurethral resection of the bladder (TURB) which is associated to intravesical BCG[ii]. However, due to state T1 aggressive behavior -mainly in its histological variants- some authors rather indicate inmediate Radical Cystectomy (RC)[iii].

Urinary bladder squamous cell carcinoma (SqCC) is the most common variant which mostly emerges in advanced medical examinations and carries a high risk of local recurrence compared to urothelial BCa[iv]. The aim of this research is for the authors to compare survival rates on patients with stage T1 SqCC who have been treated with RC versus BCG. The final outcome of it is to stablish the most effective strategy to deal with this pathology.

Retrospective analysis of 188 patients between 1998 and 2009 was conducted out of 15 reference centers. Re-TURB was conducted in one third of the patients from whom the ones suffering from RC with neoadjuvant were excluded.

The primary objective of this research was cancer-specific mortality (CSM) and global mortality (OM). As a secondary objective recurrence-free survival (RFS) and progression-free survival (PFS) were evaluated in the group of patients who were being treated with BCG treatment.

Survival results found on CSM and OM with five years of separation between RC vs BCG was 29% (95% [CI]:15-45%) vs 16% (95% [CI] 9-24%) and 34% (95% [CI] 20-53%) vs 26% (95% [CI] 18-35%]). These results show no significant difference between both survival groups. Multivariate analysis showed that pure squamous BCa were associated to a higher risk of progression (hazard ratio [HR]: 2.40; p=0.04) whereas the presence of lymph-vascular invasion (LVI) as an independent factor was mostly associated with a higher risk of both recurrence and progression (HR: 1.94; p = 0.04 and HR:2.19; p = 0.04, respectively).



Such findings suggest that RC offers no benefits on patients with T1 squamous BCa compared to the conservative treatments with BCG. These findings are consistent with the research published by Suh et al. [v], in which Ta/T1/Cis with squamous or glandular components also did not show significant difference in specific cancer survival and global survival in 5 years. The results obtained in RFS and PFS three years later were 52% y 75% respectively. These are as comparable to the ones in literature [vi], showing effectivity of the BCG treatment on squamous BCa.

It was possible to establish that the group of patients who did not present pure SqCC or LVI concomitant component benefited more from the immunotherapy treatment. Such results would allow the option of a conservative BCG treatment in patient who do not present neither recurrence-free survival nor progression-free survival factors, whereas for those who present these factors, the RC would be the chosen treatment so as to lower the recurrence and progression risk.

This study presents several limitations. First and foremost, it is bound to selection bias due to its retrospective design. Owing to its multicentric characteristics, it shows heterogeneity in schemes and BCG doses used, recurrence and progression criterium and the lack of centralized pathological anatomy revision.

Further prospective, multicentric and randomized studies will be needed in order to stablish the best treatment for this BCa histological variant which is rare in this area.

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