

Diminished efficacy of bacille calmette-guérin among elderly patients with nonmuscle invasive bladder cancer

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Objective: Bacille Calmette-Guérin (BCG) is recommended as adjunctive therapy among patients with high-risk nonmuscle-invasive bladder cancer (BC). Given that immune response is attenuated with age, we set out to determine the impact of age on response to BCG.

Materials and Methods: We searched our prospective bladder information system and limited our search to patients with incident BC completely resected at transurethral resection (TUR) who completed a full induction course of BCG. We then analyzed the impact of age on outcome. Age was analyzed both dichotomously (greater or less than 75 years) as well as by 10-year increments. The main outcomes were recurrence or progression-free survival. Log-rank and multivariable Cox proportional-hazard analyses, adjusting for clinical and pathologic features (age, multifocality, pathologic stage, grade and associated carcinoma in situ, maintenance, and restaging) were used.

Results: This cohort included 238 patients. Baseline parameters were similar aside from tumor number. Progression-free survival differed between age groups when examined either dichotomously or via 10-year increments. The 2-year progression-free survival was 87% among patients < 75 years vs 65% in patients > 75 years (log rank $P < 0.001$). An age-dependent trend was noted when analyzed by 10-year increment (log-rank for trend $P = 0.011$). On multivariable analysis, age was an independent risk factor for progression (HR = 2.9, 95% CI 1.7-4.9). Recurrence-free survival was similar among age strata.

Conclusion: We demonstrated that advanced age is associated with higher progression rates despite BCG. The care of BC in the elderly population is of increasing concern and should be addressed in a prospective clinical study.

Editorial Comment

The only independent risk factor for progression in this cohort was age (≥ 75 years vs < 75 years) with a HR of 2.1 (95% CI 1.7-4.9), and maintenance therapy resulted in a statistically significant decrease risk of progression with a HR of 0.8 (95% CI .92-.64). Maintenance therapy significantly reduced the risk of recurrence in patients younger than 75 (HR 0.76; 95% CI .93-.60) as well as those older than 75 (HR 0.86; 95% CI .99-.60).

Progression was associated with age, even after controlling for BCG maintenance and re-resection in a very homogenous cohort where all patients had newly diagnosed bladder tumors (primary presentation), and that completed a full induction course of intravesical BCG, the only clinically used adjuvant therapy known to decrease progression. However data should be viewed with caution given the retrospective design, the unavoidable selection bias and the relatively small cohort.

It was previously suggested that elderly are more commonly exposed to statins and fibrin clot inhibitors (aspirin or coumadin); these exposures are known to alter BCG response. On the other hand, a worse pathophysiology could not be excluded in elderly and was previously proposed by others, although these studies are also deemed to selection bias (1).

Future studies are necessary to confirm these findings and to optimize cancer treatment of elderly.

Reference

1. Fairey AS, Kassouf W, Aprikian AG, Chin JL, Izawa JI, Fradet Y, et al.: Age \geq 80 years is independently associated with survival outcomes after radical cystectomy: Results from the Canadian Bladder Cancer Network Database. *Urol Oncol.* 2011; 1. [Epub ahead of print]

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