Locally-advanced prostate cancer in the elderly: should we revisit our treatment paradigms?

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Prostate cancer (PCa) represents the most common malignancy in adult males with an estimated number of 280 000 newly diagnosed cases only in the United States in 2015. Due to the introduction of PSA in clinical practice, the majority of the patients are currently diagnosed with organ-confined and sometimes indolent disease. However, a nonnegligible proportion of individuals are still diagnosed with locally-advanced tumors. In their recently published article, Bekelman et al. focused on elderly patients with locally-advanced PCa in the attempt to determine the best treatment approach in this patient category, and concluded that, even in these individuals, androgen deprivation therapy (ADT) plus radiotherapy (RT) may confer a survival benefit relative to ADT alone. The importance of the current article resides in the fact that it focuses on a patient population that has not been, or has been only scarcely, included in previous studies on the same topic.

The survival benefit of RT plus ADT versus ADT alone in patients with locally-advanced PCa has been recently demonstrated by two randomized controlled trials (RCTs). Specifically, Widmark et al. recruited 875 patients from 47 Scandinavian centers who were randomized to receive either ADT or ADT plus RT. Inclusion criteria for this study were age ≤75 and a life expectancy ≥10 years. According to this criteria defined by the two previously cited studies; (2) the elderly cohort (n = 14,340), consisting of men aged between 76 and 85 years with locally-advanced PCa; (3) the screen-detected cohort (n = 4277), consisting of patients aged between 65 and 85 years with high-risk clinically undetectable disease. Besides standard survival analysis, the authors also adopted two statistical methodologies, namely the propensity score approach and instrumental variable analysis in order to adjust for possible confounders. In all of the three scenarios (unadjusted, propensity-score and instrumental variable adjusted), ADT plus RT resulted in a significant increase both in cancer-specific and overall mortality rates as compared to ADT alone. Interestingly, the survival benefit was observed not only in the RCT cohort, but also in the elderly and in the screen-detected ones. In consequence, this study provides evidences to expand the indications for ADT plus RT also to these patients. This is even more important when considering that, despite the potential survival benefits, older patients with locally-advanced PCa are less likely to receive local therapies relative to their younger counterparts.

However, while the population-based nature of this study may support the generalizability of its findings, it also represents a potential limitation that should be taken into account when interpreting the results. As correctly stated by the authors, several important data, such as total PSA and radiation dose/field, were missing. The retrospective nature of the dataset along with the risk of a misclassification bias also represents a limitation. In addition, no information was provided regarding the toxicities of ADT plus RT versus ADT alone and whether differences in the rate of side effects existed between the three groups. Finally, the oncological outcomes and morbidities of ADT plus RT in locally-advanced PCa should also be compared to those of radical prostatectomy with or without adjuvant RT, especially in carefully selected patients with a life expectancy ≥10 years.

In conclusion, the study by Bekelman et al. adds important evidences regarding the oncological effectiveness of ADT plus RT relative to ADT alone in locally-advanced PCa even in older individuals. However, the clinical applicability of their findings should be further corroborated by prospective randomized trials focusing on this patient category.

COMPETING INTERESTS
The author declares no competing interests.
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