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COMMENTARY

Adjuvant Radiation for Locally Advanced Bladder Cancer? A Question Worth Asking

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Introduction

In the article that accompanies this commentary, Reddy et al (1) report the results of a painstaking review of risk factors for, and locations of, pelvic failure after radical cystectomy for locally advanced bladder cancer and discuss their implications for adjuvant radiation. This work considers a cohort of patients with pT3-4, N0-1 disease for whom outcomes are poor—a 3-year overall survival of 39% in this study—and for whom there has been no meaningful advance in nearly 2 decades. Promisingly, this is also an area of intense international interest. Encouraged by foundational work from the National Cancer Institute in Egypt (2), groups in North America (NRG Oncology), France (GETUG-AFU), the United Kingdom (NCRI), and India (Tata Memorial Hospital) have already opened, or are in the process of developing, clinical trials of adjuvant radiation. Herein, we review where the results reported by Reddy et al (1) are consistent with the existing literature and where they raise new questions.

Which Patients are most Likely to Benefit?

Investigators use risk of pelvic failure as a surrogate for which patients are most likely to benefit from adjuvant radiation. The most rigorously tested risk stratification separates radical cystectomy patients into 3 subgroups based on pT stage, serosal surgical margin status, and the number of benign or malignant lymph nodes identified within the pelvic lymphadenectomy specimen (Table 1) (3). This model effectively stratified pelvic failure risk in at least 4 diverse radical cystectomy cohorts: retrospective institutional series from the United States (3) and South Korea (4) and prospective multi-institutional series from North America (3) and Europe (5). In addition, the absolute pelvic failure estimates from these heterogeneous datasets were remarkably similar, with 5-year pelvic failure rates of approximately 8% for low-risk, 19% to 21% for intermediate-risk, and 41% to 46% for high-risk groups (Table 1). Thus, the existing literature suggests that this model is robust to temporal and regional variations in patient cohorts, surgical technique, and pathologic assessment.

The report by Reddy et al (1) is an interesting addition to the risk factor literature, in part because it provides insight into the role that these clinical variables play at a very high-volume tertiary care center. In their risk factor analysis, Reddy et al (1) report that only pT stage and pN stage were significant independent predictors of pelvic failure. The relationship of pT stage to pelvic failure is consistent with the existing literature. The relationship of pN stage is clinically plausible, but the existing research is mixed about its effect. Different conclusions in the literature may be the product of varying statistical methods. The validated stratification summarized in Table 1 was developed by the use of cumulative incidence functions, with isolated distant

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Conflict of interest: J. Christodouleas reports employment at Elekta, Inc. The other authors report no conflict of interest.

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