High Risk Populations and Cystectomy Outcomes

Radical cystectomy with pelvic lymph node dissection is standard treatment for muscle invasive and refractory or recurrent nonmuscle invasive urothelial cell carcinoma. The survival of patients undergoing radical cystectomy is variable and dependent on multiple prognostic risk factors. Better prognostication and risk stratification are needed to assist with treatment planning, patient counseling and clinical trial design. Two studies in this issue of The Journal address prognostication of survival outcomes for patients undergoing radical cystectomy for urothelial cell carcinoma. Isbarn et al (page 70) and Fairey et al (page 85) use distinctly different study designs to identify preoperative prognostic factors associated with outcomes for patients undergoing radical cystectomy, and we review some of the strengths and weaknesses of these different methodologies.

Perioperative mortality is a devastating outcome for families and surgeons of patients undergoing radical cystectomy.1 Predicting those patients at highest risk for perioperative mortality is critical in identifying potentially preventable causes and in guiding clinicians regarding which patients to consider for alternative treatment options. A limited number of reports have specifically addressed the role of prognostic information for this outcome. Isbarn et al used the population based SEER (Surveillance, Epidemiology, and End Results) carcinoma registry data to test the prognostic value of age, gender, stage, grade, type of surgery (partial vs radical cystectomy), year of cystectomy and histological subtype with perioperative mortality. They reported that nontransitional cell carcinoma subtype, advanced age, grade and stage were independently associated with 90-day mortality after cystectomy. In addition, they quantified mortality rates at different assessment times after surgery, and found that the 30, 60 and 90-day perioperative mortality rates were 1.1%, 2.4% and 3.9%, respectively.

There are several limitations to the results drawn from SEER data that are relevant to this analysis, and include underreported or incomplete data, lack of coding reliability, variations in data reporting among registries, and migration of patients in and out of registries. In addition, the major causes of perioperative death for patients undergoing radical cystectomy are cardiovascular related morbidity or systemic consequences of sepsis, both of which are directly related to variables not captured from SEER data registries, namely patient comorbidity status and hospital/surgeon procedural volume.1 The influence of these covariates undoubtedly contributes to the authors’ inability to explain a considerable portion of the variation in perioperative mortality in the study as the prediction rule failed nearly 30% of the time.

Notwithstanding those limitations this work has the strength of being a large, nationally representative, population based study. The authors used the highest quality standards for statistical modeling along with independent, external validation. The nomogram that accompanies the article provides an accurate perioperative mortality prediction in 7 of 10 patients undergoing cystectomy and represents a major advance in the prognostication of early mortality for these patients. In addition, by assessing perioperative mortality at various points after cystectomy the authors emphasize the importance of assessing perioperative mortality at least 90 days after surgery.

In contrast to the national population SEER based study Fairey et al used a comprehensive clinical data set obtained from a single health region in Edmonton, Canada. They evaluated the association of comorbidities with overall and disease specific survival after radical cystectomy, and they observed that increased comorbidity status was independently associated with overall and bladder cancer specific survival after adjusting for competing clinical and pathological characteristics. Patients with no or mild comorbidity status experienced a significantly higher 5-year estimated overall survival rate (65%) compared to those with a moderate (51%) or severe (47%) comorbidity status.

The main strength of this study lies in the quality and comprehensiveness of the available data, which allow the use of a chart based comorbidity scale that addresses the full range of comorbid conditions commonly found in patients with carcinoma, while permitting adjustment for the con-
founding effects of surgeon procedure volume as well as lymphadenectomy status and surgical margin status. In addition, the study used validated comorbidity instrumentation and chart based rather than claims based data. The main study limitation is that only patients from a single province were evaluated, which may potentially limit the generalizability of the findings to the populations of other regions. In addition, the limited number of patients and events in the cohort constrain the precision of the estimates, particularly for the 10-year survival estimates in which only 2 patients with a severe comorbidity status were at risk for death.

These articles provide valuable predictive information for patients undergoing radical cystectomy and underscore the need for improvement in prognostication. We anticipate that further elucidation of the underlying biology and mechanisms of bladder cancer initiation and progression will guide biomarker development and improve our current predictive models.

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