Prognostic tools for esophageal cancer: “Looking for the crystal ball”

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Central Message

This systematic review demonstrates that published predictive models for esophagectomy do not meet currently accepted criteria. Gupta et al. provide a benchmark for testing future prognostic models.

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Options for treating esophageal cancer have expanded considerably and incorporate more “personalized” multimodal approaches that include consideration of not only neoadjuvant treatment but also newer targeted therapies.^{1,2} As treatment has evolved, the development of meaningful prognostic tools has lagged in response to such strategies. Systematic evaluations of other prognostic tools, such as those for colorectal cancer, highlight the challenges of developing reliable risk models.³ With limited guidance on the quality of similar tools in esophageal cancer, clinicians are left to consider each new published nomogram or predictor without any information about how one tool might work better than the next in terms of risk and outcome prognostication. Clinicians are left with a very basic question: beyond the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control cancer staging criteria, are there any reliable prognostic algorithms for long-term outcomes in esophageal cancer?

In their systematic review in the *Journal*, Gupta and colleagues⁴ have taken on the task of addressing this question, and they identified significant gaps in the quality of published predictors. Using the AJCC criteria for developing risk models, the authors identified current prediction tools for esophageal cancer treatment outcomes. They applied the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines as well as the Critical Appraisal and Data Extraction for Systematic Reviews of Predictions Modeling Studies (CHARMS) checklist to evaluate study validity.⁵⁻⁷ Among 16 reported risk models, the authors observed significant heterogeneity in the included covariates; only one model, in their opinion, captured a majority of significant variables. Their study found that many tools were derived from patients with esophageal squamous cell carcinoma, excluding other histologic subtypes, particularly adenocarcinoma. In addition, the identified predictors did not always include current clinical practices (eg, consideration of neoadjuvant therapy) and excluded

clinically relevant factors, such as cancer stage, patient age, and sex, that had been long associated with outcome after esophageal cancer treatment.⁴

Although Gupta and colleagues established that most relevant published risk models do not meet currently accepted criteria as outlined by the AJCC, TRIPOD, and CHARMS schema, they acknowledge that most of the identified reports predated these guidelines. In addition, they observed that development of all the identified prognostic tools was methodologically sound, well-described, and used appropriate statistical analyses. Their descriptive, albeit rigorous, study does not test the basic hypothesis whether any of these published models might yet be accurate when applied to an external and contemporary patient dataset. Instead, their study emphasizes that investigators should apply guidelines, such as those published by the AJCC or outlined by TRIPOD and CHARMS, when seeking to develop prognostic tools that will be applicable to the current practice of esophageal cancer surgery. This will be particularly important as we venture toward a more personalized approach to treating esophageal cancer that includes not only multimodality treatment but also targeted therapies seeking to exploit tumor-specific molecular aberrations.

Although existing predictors provide only rough estimates of oncologic and surgical outcomes, when developing future tools, investigators should consider including

not only well-established prognostic factors but also molecular diagnostic information. Such tools would help inform decision-making for both the clinician and the patient, keeping pace with evolving diagnostic and treatment practices for this lethal disease.

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