Imaging and scopes? It's bloody time for another branch in the decision tree

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Central Message

To wait or to resect after chemoradiation therapy for esophageal squamous cell carcinoma? Where are the biomarkers?

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So many challenges in the management of esophageal cancer persist: high perioperative morbidity for esophagectomy, poor overall survivals, and, more recently in the era of salvage esophagectomy, selection of the optimal subset after chemoradiation. Less invasive resection approaches have reduced some of the respiratory morbidity and allowed superficial tumors to be treated endoscopically, but survivals have not improved significantly, and the idea of a watch and wait approach after chemoradiation has spared some patients the esophagectomy risks. The central message of the retrospective study by Liw and colleagues¹ in this issue of the *Journal* is that disease recurs in 50% of patients who show a complete clinical response after definitive chemoradiation for esophageal squamous cell carcinoma. This watch and wait plan needs additional direction. The literature contributions of their work are 2-fold: (1) surveillance strategies after definitive chemoradiation to identify candidates for additional treatment and (2) confirmation of clinical risk factors (stage and age) impacting disease recurrence. Their suggested surveillance protocol includes upper endoscopy every 3 months for 2 years for local recurrence and compute tomographic scan or positron emission tomographic–computed tomographic scan every 6 months for 4 years. Patients with recurrence are then offered stage-appropriate therapy. More sophisticated tests are needed to improve this algorithm for those with complete clinical response.

What are the options for improving detection of persistent gross and occult disease? Deeper biopsies on restaging and surveillance endoscopy, as suggested recently by Fujishima and colleagues²? Improved imaging with positron emission tomography–magnetic resonance imaging, as suggested by our nuclear medicine colleagues³? What about the old kid in town: blood biomarkers? For many years and for many solid tumors, investigators have detected circulating micrometastases⁴⁻⁶ or microsatellite instability in the serum⁷ and theorized a correlation with prognosis; in 2018, however, this is still not a test to be ordered through

electronic medical records. So where do we go from here? Newer investigations in our esophageal molecular research arena are potentially more promising. We have found that technical advances in digital polymerase chain reaction can improve specificity of rare event analysis⁸ and allow detection of circulating cell-free tumor DNA levels in the serum of patients with esophageal adenocarcinoma. In soon-to-be-published studies, these circulating cell-free tumor DNA levels have been shown to correlate with circulating response to therapy, recurrence, and disease progression, and increases in the circulating cell-free tumor DNA levels have been seen to precede radiographic evidence of changes in tumor behavior and in addition to correlate with tumor burden.

When will we draw the next branch on the decision-making tree for resection or no resection after chemoradiation for esophageal cancer? It may bloody well be soon.

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