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Commentary: All that glitters isn't gold: Defining low-risk lesions in early-stage esophageal adenocarcinoma

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CENTRAL MESSAGE

Among patients with T1 esophageal adenocarcinoma, those with tumors <2 cm in length without lymphovascular invasion have a low risk of recurrence.

In this issue of the *Journal*, Shihag and colleagues¹ identify risk factors for recurrence among patients with completely resected T1 esophageal adenocarcinoma. The main impetus for this analysis is the paradigm shift of treatment for early-stage esophageal adenocarcinoma away from radical esophagectomy and toward organ-sparing techniques, such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). The promise of treating esophageal cancer with endoscopy certainly has the promise of alchemy and has been supported by several retrospective institutional series demonstrating comparable overall survival between EMR and esophagectomy as long as a negative margin is achieved.^{2,3} Unfortunately, as the expression goes, all that glitters is not gold, and we must question whether EMR and ESD is the 24K magic bullet we seek for early-stage esophageal adenocarcinoma.

The analysis showed an overall survival of 68.6% at 5 years and a median interval to recurrence of 2.0 years. Most recurrences were distant, with a cumulative incidence of recurrence (CIR) of 11% for distant recurrence but only 4% for locoregional recurrence. In multivariable analysis, only pathologic N1 disease and tumor length were significant risk factors for recurrence.

Although useful, this information doesn't allow us to determine which patients may be better suited for endoscopic techniques versus esophagectomy. To that end, the team constructed a final multivariable model using

only clinicopathologic variables that may be known preoperatively. In this model, only lymphovascular invasion (LVI) and tumor length were significant. Finally, using this information, they defined a low-risk group and a high-risk group. They found a significantly higher CIR and risk of death in the high-risk group, validating their stratification.

The authors conclude that patients without LVI and tumor length <2 cm have the lowest risk of recurrence (<10%) and a 5-year survival of 75%, which may identify them as good candidates for endoscopic resection. In contrast, patients deemed high-risk (LVI or with tumors >3 cm) have a >10% risk of recurrence and may be better treated with esophagectomy.

In the end, it appears that the optimal treatment for T1 esophageal adenocarcinoma remains to be determined. Although endoscopic techniques shine and glitter as less morbid yet equally effective treatment options for patients with early-stage esophageal cancer, it may be necessary to parcel these patients based on risk of recurrence to determine who will derive the maximal oncologic benefit. Furthermore, with the rate of distant recurrence double that of locoregional recurrence, it remains to be seen if the decision will remain between two surgical techniques or, as we have witnessed in lung cancer, genetically targeted systemic therapies will evolve into the ultimate 24K magic bullet.

References

1. Shihag S, Torre SDL, Hsu M, Nobel T, Tan KS, Gerdes H, et al. Defining low-risk lesions in early-stage esophageal adenocarcinoma. *J Thorac Cardiovasc Surg*. 2021;162:1272-9.

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<https://doi.org/10.1016/j.jtcvs.2020.11.144>

2. Ramay FH, Vareedayah AA, Visrodia K, Iyer PG, Wang KK, Eluri S, et al. What constitutes optimal management of T1N0 esophageal adenocarcinoma? *Ann Surg Oncol*. 2019;26:714-31.

3. Marino KA, Sullivan JL, Weksler B. Esophagectomy versus endoscopic resection for patients with early-stage esophageal adenocarcinoma: a national cancer database propensity-matched study. *J Thorac Cardiovasc Surg*. 2018;155:2211-8.

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Commentary: Risk stratification for superficial esophageal adenocarcinoma: Reducing risk in a risky business!

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Organ preservation in the treatment of early esophageal cancer is an accepted paradigm. These techniques are appropriate for carefully selected patients who have early-stage and less aggressive tumors or as a mitigating measure.¹ Unlike some other malignancies for which the aggressiveness of the cancer, such as lung cancer, can span the spectrum of indolent to aggressive, esophageal adenocarcinoma mostly has aggressive and very aggressive biology. As such, only the earliest of cancers have a low enough risk of metastatic spread at the time of diagnosis that they can be treated with local therapies. However, the identification of this “low-risk” population has remained elusive.

In their article, Sihag and colleagues² have attempted to define criteria associated with a low risk of cancer recurrence in pT1 esophageal adenocarcinoma. In the univariable analysis, they identified the usual suspects for increased risk, such as submucosal invasion, poor differentiation, nodal disease, increased tumor length, and multicentricity. However, using a multivariable model, the authors have demonstrated only increased tumor length and nodal disease to be independent risk factors for recurrence. More interestingly, they set out to identify cancers

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CENTRAL MESSAGE

Early-stage esophageal cancer may be amenable to endoscopic therapy, but requires careful assessment of cancer characteristics.

with less than 10% chance of recurrence on the basis of only preoperative clinicopathologic features. In doing so, they noted that patients with tumors less than 2 cm without lymphovascular invasion had a low rate of recurrence.

It is important to note that the patient population identified in the study includes those with completely resected cancers in whom recurrence status was retrospectively explored. Given that they have had a reasonable nodal dissection, occult metastatic disease (be it in regional lymph nodes or in transit within the esophageal lymphatics) may have been surgically removed in clinically node-negative patients. It is difficult to determine how these results would translate to recurrence in patients after endoscopic resection only in whom a lymphadenectomy had not been performed. Additionally, the authors only found N1 disease to be significant but not depth of invasion or poor differentiation to be a risk factor for recurrence. Although curious at first glance, it is likely because their study population was small, and these, at some level, are related variables.

This original work² adds to our current knowledge base about tumors that are low risk, high risk, and everything in between. Mucosal tumors without poor differentiation or lymphovascular invasion are clearly suited to organ-

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