The role of local excision in invasive adenocarcinoma of the ampulla of Vater

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The provocative article by Zhong et al. considers an unusual subset of patients from their extensive experience at Duke University undergoing open ampullectomy for adenocarcinoma of the ampulla of Vater (1). These patients would have typically undergone pancreaticoduodenectomy, but due to prohibitive comorbidities or patient preference underwent surgical ampullectomy instead. Given the infrequency of open ampullectomy for malignancy in their practice (only 17 patients over 35 years), we appreciate the authors judicious use. Nevertheless, there is some evidence that patients with early stage invasive disease could be treated by local resection with reasonable outcomes (2). In the current study, T1 tumors were associated with a 40% 5-yr survival. The potential use of local resection for early stage disease in patients with prohibitive operative risk becomes even more intriguing when one considers the increased use and acceptability of endoscopic ampullectomy (3).

We agree with the authors that the standard of care for ampullary adenocarcinoma continues to be radical resection with lymphadenectomy. This is based on the substantial risk of lymph node metastases and positive margins associated with local resection, especially for T2 lesions and above. Not unexpectedly, there is some evidence that patients with early stage invasive disease could be treated by local resection with reasonable outcomes (2). In the current study, T1 tumors were associated with a 40% 5-yr survival. The potential use of local resection for early stage disease in patients with prohibitive operative risk becomes even more intriguing when one considers the increased use and acceptability of endoscopic ampullectomy (3).

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The authors address another important and very practical question of whether chemoradiation is beneficial after local resection. The authors demonstrate a 76% local failure rate at 5 years despite a 5 year metastasis free survival of 54%. Clearly, patients are succumbing to local disease, a situation where aggressive loco-regional adjuvant therapy would intuitively appear beneficial. Two recent studies have demonstrated a benefit to ampullary cancer patients who received adjuvant therapy following pancreaticoduodenectomy (5,6). Preliminary data from the large randomized ESPAC-3 trial suggests survival benefit for chemotheraoy alone while the Johns Hopkins-Mayo Clinic retrospective study demonstrated a survival benefit to adjuvant chemoradiation. While the present study was not able to show outcome benefit with chemoradiation, the authors do acknowledge the very small sample size and the disproportionate number of patients with positive margins and poorly differentiated tumors.
in the chemoradiation group. Also, adjuvant therapy did not include a chemotherapy alone component, which is common in current adjuvant strategies for periampullary cancers. For patients who are clearly not candidates for pancreaticoduodenectomy and have ampullary tumors amenable to local resection, endoscopic or surgical ampullectomy and adjuvant chemoradiation still appears a rational option.

Zhong et al. note the high (47%) margin positivity rate associated with surgical ampullectomy for cancer and the inability to appropriately stage patients with lymphadenectomy. The technique used in this study is described as a mucosal resection incorporating the ampulla of Vater with reconstruction of the bile and pancreatic ducts and duodenal mucosal advancement. Surgical ampullectomy can be extended deeper, even full thickness into the pancreas. This may have averted some of the cases of margin positivity, although we are not given information on the specifics of margin assessment. Given the significant comorbidities and poor performance status of this patient cohort, the authors may have conscientiously wished to mitigate risk by not pursuing more aggressive surgical ampullectomy. Predicting T-stage and the potential for a positive margin, together with information regarding adverse pathologic factors (e.g., lymphovascular invasion or poorly differentiated tumors), may be helpful in the evaluation process for surgical ampullectomy in high risk patients. The use of endoscopic ultrasound and endoscopic ampullectomy could provide this additional information and potentially spare patients with more advanced local disease an invasive procedure with little hope of long-term benefit and measurable risk.

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References
