Editorial

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, the use of local excision for ampullary adenocarcinoma in the present study resulted in a considerably higher rate of 5-yr local disease recurrence (76%) and worse 5-yr survival (21%) compared to standard pancreaticoduodenectomy (4). When faced with similar patients who are not candidates for radical resection, our group will give consideration to surgical or endoscopic local resection, based on technical feasibility and acceptable risk. Every effort is made for accurate risk assessment and patient optimization prior to excluding radical resection as an option.

Since the implication in this study was that many of the patients were not suitable operative candidates for pancreaticoduodenectomy, it would have been helpful for the authors to elaborate on the "rare" postoperative complications. A recent study from the same institution comparing endoscopic to surgical ampullectomy for primarily pre-malignant disease demonstrated morbidity for endoscopic resection of 18% compared to 42% for open resection (3). Especially noteworthy was the comparison of operative morbidity for surgical ampullectomy (42%) to pancreaticoduodenectomy for benign disease (47%). Surgical ampullectomy remains a major surgical endeavor and for most surgeons, an operation they will have much less experience with than pancreaticoduodenectomy. The operative risk of surgical ampullectomy in a patient with severe comorbidities or poor performance status should not be taken lightly. With greater experience and availability of interventional endoscopy we may see a shift away from surgical ampullectomy towards increased use of endoscopic resections. In patients with significant operative risk this may provide the most favorable balance of risk and benefit.

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 chemotherapy 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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