



Minimally invasive liver resection for gastric cancer liver metastases

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For most of the last century, gastric cancer (GC) has been one of the leading causes of cancer related deaths worldwide (1). Although its incidence has significantly declined, it remains a major cause of morbidity and mortality in the United States and worldwide (2,3). Due to advances in surgical management, the prognosis has improved for patients with early stage disease amenable to surgical or endoscopic resection. Indeed, some Eastern countries with a high incidence of GC have initiated screening programs to aid with early identification. In the West, however, screening programs are uncommon, thus most patients present with advanced disease, including approximately 50% with distant metastases (4,5). The outcomes of these patients, treated with non-surgical therapies, have traditionally resulted in a 5-year relative survival rate of less than 5%. Surgical resection, when performed, was solely for palliation with little or no role for metastasectomy (6,7).

Over the last two decades, there has been accumulating evidence that resection of oligometastatic disease may lead to improvements in the overall survival of well selected patients with a variety of cancers (8,9). For example, resection of colorectal liver metastasis is well established, and combined with modern systemic chemotherapy, results in extended survival durations. On the other hand, resection of gastric cancer liver metastasis (GCLM) has traditionally been rarely indicated due to the poor prognosis associated with advanced stages of the disease and the fact that oligometastatic disease is relatively rare for GC (9,10). Nevertheless, there has been increasing interest in

identifying patients with limited metastatic disease from GC who might benefit from metastasectomy. In fact, several case reports and multi-institutional retrospective studies have reported improved outcomes among select patients undergoing resection of GC metastases in conjunction with systemic chemotherapy (10,11). However, the REGATTA trial, which randomized patients with oligometastatic synchronous disease to either chemotherapy alone versus gastrectomy (but not metastasectomy) followed by chemotherapy, demonstrated no improvement in survival with the addition of surgical resection (12). The RENAISSANCE (AIO-FLOT5) trial is a prospective randomized control trial that will seek to clarify the role of surgery for the primary and metastatic disease in patients with chemotherapy responsive advanced GC (13).

For those patients selected for resection of their GCLM, the optimal surgical approach has not been established. The use of minimally invasive liver resection (MILR) has existed since the early 1990s (14,15), however, its adoption has been slow, owing to the technical challenges associated with the procedure. Nevertheless, with improvements in surgical technology as well as enhanced education and training, the use of MILR continues to increase. This has permitted the extension of traditional benefits of laparoscopic surgery such as decreased blood loss, improved pain control, shorter length of hospital stay, and reduced overall complication rates, to be applied to patients undergoing liver resection. Furthermore, MILR for malignant tumors (including metastatic lesions) has been shown to have comparable oncologic outcomes to open resection (16). For example,

MILR of colorectal liver metastasis is associated with similar margin negative resection rates and recurrence-free survival (17).

In a recent study, Li *et al.* (18) recently compared the outcomes of patients with GCLM undergoing open versus minimally invasive resections. The researchers reviewed 53 cases of GCLM undergoing radical gastrectomy combined with hepatectomy and/or radiofrequency ablation (RFA) between 2006 and 2016 at a single large Chinese institution. After propensity score matching, they noted a significantly shorter operating time, reduced estimated blood loss, and less time to diet advancement among patients undergoing MILR compared with patients who underwent open resection. Other short- and long-term outcomes were similar between the groups. The authors, therefore, concluded that MILR was the preferred approach for resection of GCLM when feasible.

The feasibility of MILR for metastatic disease has been well documented (19). It is, thus, not surprising that Li *et al.* found similar outcomes with respect to the technical feasibility of this approach. The biology of GC, however, differs greatly from colorectal cancer, and, as such, the indications for resection are not necessarily translatable. The primary challenge, therefore, in the surgical management of GCLM is not the technical feasibility of the procedure, but the ability to identify which patients are appropriate for resection. Unfortunately, this analysis provides limited insight on this issue. First, most of the patients in the study did not receive preoperative systemic chemotherapy, which is a critical component of the multidisciplinary care of both localized and metastatic GC at most major centers (11). The absence of systemic chemotherapy makes it difficult to interpret the optimal selection of patients for resection of GCLM. Second, the true impact of metastasectomy is difficult to conclude as many patients were treated with RFA with or without resection. Finally, all patients in this study had synchronous disease, meaning that the short-term benefits observed could be a result of minimally invasive gastrectomy (20); whether these outcomes are reproducible among patients with metachronous disease is unknown (21).

Li *et al.* should be commended on their excellent outcomes performing MILR for GCLM. However, the current study fails to address the most important question facing this challenging population: which patients are most suitable for resection, open or minimally invasive, of their GCLM? Not surprisingly, previous studies have shown that young age, few metastases, response to chemotherapy

and complete margin negative resection represent the best prognostic factors. For example, Kinoshita *et al.* performed a large multi-institutional review of 256 patients with GCLM undergoing resection and showed that three or more metastases, tumor size >5 cm and primary tumor serosal invasion were major prognostic factors influencing survival (22). In a recent systematic review by Liao *et al.*, poor response to chemotherapy was noted to be associated with significantly worse survival, in addition to the other factors such as performance status, liver function and ability to achieve complete resection (23).

In summary, the surgical management of GCLM remains a challenging issue. Evidence from retrospective cohort studies and meta-analyses has resulted in revised guidelines from the Japan Gastric Cancer Association, noting that metastasectomy is acceptable for selected patients with resectable oligometastatic disease (24). However, randomized controlled trials are lacking and therefore further research on the appropriateness of hepatectomy for GCLM is greatly needed. Nevertheless, when indicated, MILR appears to be an acceptable if not preferred surgical approach among appropriately selected patients that maximizes short-term outcomes and results in similar oncologic outcomes compared to traditional open resection.

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