

Surgical resection of gastric cancer hepatic metastases: expanding the indications for curative treatment

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We would like to thank Tiberio *et al.* (1) for their editorial in response to our review entitled, "Influence of surgical resection of hepatic metastases from gastric adenocarcinoma on long-term survival: systematic review and pooled analysis" (2). The main findings of this pooled analysis of 39 studies was surgical resection of hepatic metastases improved overall survival, and an additional survival benefit of solitary compared to multiple hepatic metastases. Studies from the Far East showed a greater survival compared to those from the West. We have followed up this review with a primary study from our English National Hospital Episode Statistics database, and demonstrated in 78 patients with gastric cancer and hepatic metastases (91% synchronous) the prognostic benefit of gastrectomy and hepatectomy for metastases in selected patients (3).

Tiberio *et al.* (1) suggest that cohorts of patients observed in every-day clinical practice and not super selected populations should be submitted to surgical resection. However it is important to consider, these patients with gastric cancer hepatic metastases would normally receive best supportive treatment or palliative chemotherapy. Changing treatment approach to a curative intent would include gastrectomy, hepatectomy and neoadjuvant or adjuvant chemotherapy, representing a vast change towards an aggressive strategy.

Patient selection for such an approach involves consideration of: (I) patient physiology and (II) tumor related-factors. As Tiberio *et al.* highlight, there is a substantial drop in survival from 6 months to 1 year following surgery in most series (2-6). The majority of series included in our review (2), failed to describe cause of death in the assessment of overall survival, and thus may be due to the long-term physiological effects of surgery or

chemotherapy. Therefore the suggestion that this approach can be adopted in the average cohort of patients presenting with gastric cancer remains un-determined based on the current published literature, and patients must be selected on a case-by-case basis for this aggressive therapeutic strategy.

As Tiberio *et al.*, suggested important tumor related factors must be considered in the assessment of suitability of these patients for a curative treatment approach. Furthermore as rightly suggested by Tiberio there are separate individual prognostic factors associated with the primary gastric cancer and the secondary hepatic metastases. T stage of the primary gastric cancer and in particular T4 stage is considered a negative prognostic factor and a contraindication to this type of surgical approach by most centers due to the risk of peritoneal disease. Prognostic factors regarding the secondary hepatic metastases are concerned primarily with the ability to achieve an R0 resection margin as this remains a highly important factor influencing survival (4). Therefore we agree with Tiberio *et al.*, that this reaffirms the concept of hepatic metastases being included within regional disease and benefiting from regional surgical resection. However, clearly research is needed to improve understanding at a biologically level and the development of novel prognostic molecular factors from the primary gastric cancer that influence the pattern of metastases and recurrence. It is only through a scientific approach such as this that patient- and tumor-tailored treatment can provide allocation of appropriate patients who will benefit, to this aggressive curative treatment strategy. Despite the assertion by some clinicians that metachronous metastases are less biologically aggressive with a better prognosis, in our pooled analysis we

were unable to demonstrate a difference in survival between synchronous and metachronous gastric cancer hepatic metastases (2).

Most research in this area has been focused on the survival benefits associated with surgical resection of hepatic metastases from gastric cancer. However as we have described above these patients would typically be palliated and thus a change in strategy includes gastrectomy, hepatectomy and chemotherapy. It will become increasingly important for future researchers to consider the quality of life and functional recovery of these patients in addition to the survival effects. Quality of life from cancer resection is becoming an increasingly important issue concerning survivorship. The cumulative effect upon quality of life of gastrectomy, hepatectomy and additional chemotherapy must be evaluated before this treatment approach can be advocated for the majority of patients with advanced gastric cancer and hepatic metastases.

A further consideration regarding this type of approach is the surgeon and hospital-related factors that may influence outcome. The benefits of centralization of high-risk cancer surgery to high volume centers and high volume surgeons has previously been demonstrated (7,8). Cancer centralization in the past has been based upon hospital and surgeon procedural volume and the influence this has upon short-term mortality (7,8). Clearly as patients must be selected for this type of approach, so must the surgeons and hospitals undertaking this type of surgery, with principles of maintaining a low rate of perioperative mortality, radical D2 lymphadenectomy and most importantly a high rate of R0 resection margin for both surgical procedures.

At present the published literature would suggest in selected patients there may be a prognostic benefit to the resection of hepatic metastases from gastric cancer. However in the absence of randomized data, with largely heterogeneous indications employed for this radical surgical approach from the non-randomized studies to date, patient and tumor selection criteria for this type of approach requires further robust investigation. Randomized controlled trials are required to fully evaluate the role of resection of hepatic metastases from gastric cancer; given the relatively low incidence of eligible patients an international collaborative approach will be necessary to conduct such a trial. Clearly there is a lot of research to be undertaken in this area including further assessment of molecular prognostic factors and quality of life effects; however this remains a promising area of expanding the curative indications in the management of

advanced gastric cancer.

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Footnote

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