

Does Liver Resection Provide Long-Term Survival Benefits for Breast Cancer Patients with Liver Metastasis? A Question Yet to Be Answered

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Received: June 10, 2014

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The authors have no financial conflicts of
interest.

To the Editor:

We read with great interest the study by Kim, et al. titled “Does Liver Resection Provide Long-Term Survival Benefits for Breast Cancer Patients with Liver Metastasis? A Single Hospital Experience”.¹ We congratulate them for their insightful question and for publishing their experience and perspective. They studied 2176 breast cancer patients that underwent treatment in their institution, of which 110 had liver metastases and 13 received liver resection (R0 resection where possible). They concluded that liver resection resulted in improved survival, particularly in fit patients with solitary liver metastasis.

This conclusion is not well established nor substantiated by their results, as causality cannot be determined in their study design. The limitations of many similar breast cancer liver metastases (BCLM) series are attributed to their retrospective nature and the lack of a well-matched cohort of BCLM patients treated with the best medical therapy; furthermore, most studies are pure surgical series resulting in selection and publication biases as major limitations.²⁻⁴ There are no prospective randomized data to date to answer whether resection of BCLM is beneficial and to determine causality.^{4,5}

With the improvement in modern chemotherapeutics for metastatic breast cancer, unavoidably more patients are being referred for surgical opinion. The prolongation in survival demonstrated by these surgical case series may be largely attributed to more effective medical therapy rather than surgery alone. Therefore, assuming that the natural history of breast cancer has not changed, the survival trends reported in the metastatic setting could be attributed to therapeutic advances incorporating the use of hormonal and targeted therapies in palliative management, possibly further improved with surgery in well-selected patients.⁶ However, it is impossible to differentiate the specific survival benefit of surgery for BCLM from that of the modern effective hormonal or targeted chemotherapy from the current data.

Unfortunately, the report is limited by several other factors. The authors compared the patients with solitary BCLM to a group with extrahepatic as well as isolated BCLM and demonstrated that there is a significant recurrence-free survival

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and overall survival difference. It is puzzling that the difference in median survival, the most representative survival parameter, is not reported. Moreover, this observation is not surprising as the biology and disease burden of these two groups of patients are distinct. It is unclear how these observations led the authors to conclude that surgery resulted in improved survival for the patients with solitary BCLM and not the other confounders.

There are additional deficiencies that deserve to be addressed in their study: 1) Selection bias is inherent in retrospective studies; what were their selection criteria for metastectomy in their metastatic breast cancer patients? 2) What was the definition of the solitary BCLM group, which included a patient requiring three separate wedge resections in addition to an ablation? 3) The authors stated that “all patients with extrahepatic metastatic disease were treated with curative intent for their extrahepatic metastatic lesions.” We are interested to know what curative treatment was performed for extrahepatic disease such as the bone, brain, and nodal metastases and the rationale behind such aggressive policy. 4) Resection margins are reported as one of the negative prognostic factors for liver resection of BCLM; what were their resection margins, and what was the definition of the event for recurrence-free survival in both groups? 5) In isolated BCLM patients, poor prognostic factors previously reported include Estrogen Receptor-negative primary and metastatic tumors, Human Epidermal growth factor Receptor 2-negative metastases, ≥ 2 liver metastases, < 50 years old at metastasectomy, a positive liver resection margin, and hormone refractory disease.^{4,7} What was the hormonal status of patients’ BCLM and the hormonal conversion rate between patients’ primary tumor and liver metastases, and was that information taken into account with regards to treatment decisions?

Biology is king and trumps patient selection as well as surgical efforts despite the best of intents. Opponents of sur-

gical resection of non-colorectal non-neuroendocrine liver metastases, specifically for oligometastatic breast cancer, will argue that if a well-matched cohort of isolated BCLM patients is appropriately treated with modern effective medical treatment such as trastuzumab (Herceptin, Roche, South San Francisco, CA, USA), the benefits of surgery may not seem so clear or may even disappear.

Hence, it is premature to state that resection of BCLM even in selected patients has survival benefits. The bigger questions are yet to be addressed: is there a real benefit from surgery for oligometastatic breast cancer akin to colorectal or neuroendocrine liver metastases? If so, why and how do we best select these patients for surgery?

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