Editorial

Primary lymph node ratio and hepatic resection for colorectal metastases

Daniel Ansari, William Torén, Roland Andersson

Department of Surgery, Clinical Sciences Lund, Lund University and Skåne University Hospital, Lund, Sweden

Correspondence to: Daniel Ansari, MD, PhD. Department of Surgery, Clinical Sciences Lund, Lund University, Skåne University Hospital, Lund, SE-221 85 Lund, Sweden. Email: daniel.ansari@med.lu.se.

Provenance: This is an invited Editorial commissioned by Editor-in-Chief Yilei Mao (Department of Liver Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China).

Comment on: Ahmad A, Reha J, Saied A, *et al.* Association of primary tumor lymph node ratio with burden of liver metastases and survival in stage IV colorectal cancer. Hepatobiliary Surg Nutr 2017;6:154-61.

Submitted Jan 20, 2018. Accepted for publication Feb 07, 2018.

doi: 10.21037/hbsn.2018.02.05

View this article at: http://dx.doi.org/10.21037/hbsn.2018.02.05

Colorectal cancer (CRC) is a leading cause of death worldwide (1). The liver is the most common site for distant metastases, and approximately 50% of patients diagnosed with CRC develop hepatic metastases during the course of their disease (2). Improvements in surgical techniques, anesthesia and multimodal treatment regimens (e.g., neoadjuvant chemotherapy and portal vein embolization) have expanded the indications for liver resection (3). Hepatic resection is nowadays offered to patients previously deemed unresectable, such as those with multiple or bilobar metastases, extrahepatic disease and recurrent tumors. The 5-year overall survival rate after resection for CRC liver metastases is close to 60% at specialty units, with low perioperative morbidity and mortality (4,5).

Over the years, many prognostic scoring systems have been developed to risk stratify patients with CRC liver metastases in order optimize clinical management (6). Detailed histopathological analysis of the primary tumor is worthwhile, as it may assist in prognostic assessment of CRC patients with liver metastases (7). However, no scoring system has been sufficiently validated. Still, the tumor, node, and metastasis (TNM) classification is the gold standard to estimate prognosis and guide treatment decisions in routine clinical practice.

The N-stage of the primary tumor has been reported to be a strong prognostic factor in patients with CRC liver metastases, but the data remain inconclusive (6,7). Lymph node ratio (LNR, positive lymph nodes/examined lymph nodes) has been introduced in the hope that it may provide more comprehensive information. The definition of N-stage is affected by the extent of lymph node dissection by the surgeon and the node retrieval by the pathologist. LNR may overcome some of these limitations. However, optimal cut-off levels for LNR are debatable.

In a previous issue of *Hepatobiliary Surgery and Nutrition*, Ahmad *et al.* (8) report a clear association between primary LNR and the extent of hepatic tumor burden and survival in CRC patients. High-LNR (>0.25) was correlated with the number of liver metastases as well as bilobar disease. Furthermore, high-LNR was associated with decreased survival in patients undergoing hepatic resection.

Is CRC spread to lymph nodes a prerequisite for metastatic dissemination to the liver? Recent molecular phylogenetic analyses have shed new light on this topic (9). It was reported that lymph node and hepatic metastases have distinct origins in about 2/3 of cases, indicating that hepatic metastases can be generated independent of cancer cell deposits in the lymph node, likely by the hematogenous route (portal vein). Only about 1/3 of cases of lymph and liver metastases were reported to share a common origin.

What is then the mechanism behind the associations between lymph node involvement and hepatic tumor burden and survival seen in the study presented by Ahmad *et al.*? A theory is that metastatic dissemination to lymph nodes occurs early during tumor evolution and that seeding to distant locations requires genetic properties attained

later in the tumor evolution. This would explain why the metastatic lesions found in lymph nodes and distant locations are genetically diverse. In the minority of cases where the lesions seemed to have a common origin, the primary tumor may stochastically have acquired a genetic setup allowing dissemination to both niches.

Clearly, more research is mandated in order to understand the metastatic cascade in CRC and molecular features of primary, lymphatic and distant metastatic lesions. Further knowledge in this area may ultimately lead to more precise methods for prediction, prevention and treatment of metastatic disease.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Brenner H, Kloor M, Pox CP. Colorectal cancer. Lancet 2014;383:1490-502.
2. Zarour LR, Anand S, Billingsley KG, et al. Colorectal Cancer Liver Metastasis: Evolving Paradigms and Future Directions. Cell Mol Gastroenterol Hepatol 2017;3:163-73.
3. Ansari D, Bergenfeldt M, Tingstedt B, et al. Multimodal management of colorectal liver metastases and the effect on regeneration and outcome after liver resection. Scand J Gastroenterol 2012;47:1460-6.
4. Pawlik TM, Scoggins CR, Zorzi D, et al. Effect of surgical margin status on survival and site of recurrence after hepatic resection for colorectal metastases. Ann Surg 2005;241:715-22, discussion 22-4.
5. Tan MC, Castaldo ET, Gao F, et al. A prognostic system applicable to patients with resectable liver metastasis from colorectal carcinoma staged by positron emission tomography with [18F]fluoro-2-deoxy-D-glucose: role of primary tumor variables. J Am Coll Surg 2008;206:857-68; discussion 68-9.
6. Gomez D, Cameron IC. Prognostic scores for colorectal liver metastasis: clinically important or an academic exercise? HPB (Oxford) 2010;12:227-38.
7. Spelt L, Sasor A, Ansari D, et al. Pattern of tumour growth of the primary colon cancer predicts long-term outcome after resection of liver metastases. Scand J Gastroenterol 2016;51:1233-8.
8. Ahmad A, Reha J, Saied A, et al. Association of primary tumor lymph node ratio with burden of liver metastases and survival in stage IV colorectal cancer. Hepatobiliary Surg Nutr 2017;6:154-61.
9. Naxerova K, Reiter JG, Brachtel E, et al. Origins of lymphatic and distant metastases in human colorectal cancer. Science 2017;357:55-60.

Cite this article as: Ansari D, Torén W, Andersson R. Primary lymph node ratio and hepatic resection for colorectal metastases. HepatoBiliary Surg Nutr 2018;7(2):149-150. doi: 10.21037/hbsn.2018.02.05

