



Laparoscopic liver resection and adjuvant chemotherapy with optimal timing: a step towards survival prolongation in colorectal liver metastasis patients

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Response to: Ramanathan R, Geller DA. Minimally invasive liver resection—more evidence of oncologic advantage. *Ann Laparosc Endosc Surg* 2018;3:43.

Received: 19 August 2018; Accepted: 04 September 2018; Published: 13 September 2018.

doi: 10.21037/ales.2018.09.03

View this article at: <http://dx.doi.org/10.21037/ales.2018.09.03>

We are grateful to Dr. Ramanathan and Prof. Geller for their insightful comments on our recent study. Liver resection followed by adjuvant chemotherapy (AC) has been often performed for resectable colorectal cancer liver metastases (CRCLM), with cumulative evidences of survival benefit against systematic chemotherapy alone (1). The increasing diffusion and accumulation of evidences in laparoscopic liver resection (LLR) for CRCLM have revealed its feasibility and operative advantages compared to open liver resection (OLR) such as less intraoperative blood loss, lower or equal morbidity, and shorter postoperative hospital stay (2,3). Recently, a randomized control trial (RCT) showed that LLR was significantly associated with less postoperative complications and short length of stay compared to OLR in patients underwent parenchyma-sparing resection for CRCLM (4).

These findings prompted to reveal the oncologic advantage of LLR for CRCLM. Here, the survival benefit of early return to AC has been pointed out in various studies for large cohorts (5,6). Two studies have evaluated the impact of LLR on the duration between operation and AC initiation. Mbah *et al.* analyzed major liver resections including approximately 40% of metastases from other origin than colorectal cancer (7). Tohme *et al.* showed LLR was an independent contributor on early return to AC, however the collinearity between the occurrence of complications and the use of mini-invasive surgical technique was not addressed in multivariate analyses (8). Considering the influence of these analysis methods on

AC initiation, further investigation has been required to ensure the advantage of LLR for CRCLM on AC with appropriate timing. In our current study, the superiority of LLR on AC timing than OLR was also confirmed in the whole population. Moreover, the propensity score-based analysis allowed to analyze statistically matched 22 LLR and 44 OLR patients with CRCLM in terms of baseline, oncological, and intraoperative findings, and reinforced the evidence by demonstrating the advantage of LLR on AC start timing independently from confounding factors (9).

To reveal the underlying mechanism between LLR and postoperative early recovery, we further examined the postoperative laboratory data including inflammatory cytokines. However, no significant difference was confirmed between LLR and OLR groups in our study. Considering the comparable postoperative hospital stay between two groups, less invasiveness of LLR might mainly contribute to accelerate the rehabilitation after discharge, and then allow to initiate AC with the appropriate timing. In the Oslo laparoscopic versus open parenchymal liver resection for colorectal metastases (OSLO-COMET) RCT, LLR group showed significantly higher health-related quality of life (HRQOL) score than OLR group (4). Although the duration between operation and AC start was not evaluated in the RCT, HRQOL score would reflect the early rehabilitation after LLR for CRCLM. Further studies are required to identify the objective indicator of early recovery after LLR for CRCLM. Objective assessments of postoperative rehabilitation would enable to provide seamless cancer

treatments including AC without delay for CRCLM patients.

Although the solid evidence of survival benefit provided by AC after liver resection for patients with CRLM has not been fully established, it is currently evaluated in the ongoing clinical trials including a randomized phase II/III trial (JCOG0603) comparing postoperative survival of liver resection for CRLM followed by mFOLFOX6 with liver resection alone (10). Development of LLR for CRLM and cumulative evidences have shed light on the oncologic advantage as well as surgical outcome. Future prospective multi-institutional studies will achieve the prolongation of survival after LLR followed by AC with appropriate timing in CRLM patients. Finally, we appreciate again for the valuable comments provided by Dr. Ramanathan and Prof. Geller.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Laparoscopic and Endoscopic Surgery*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/ales.2018.09.03>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/ales.2018.09.03

Cite this article as: Kawai T, Scatton O. Laparoscopic liver resection and adjuvant chemotherapy with optimal timing: a step towards survival prolongation in colorectal liver metastasis patients. *Ann Laparosc Endosc Surg* 2018;3:74.