



Adjuvant chemotherapy without delay, an oncologic advantage of laparoscopic liver resection for colorectal liver metastases

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Response to: Beppu T, Imai K, Kinoshita K, *et al.* Can laparoscopic liver resection for colorectal liver metastases provide early initiation of adjuvant chemotherapy? *Ann Laparosc Endosc Surg* 2018;3:35.

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

doi: 10.21037/ales.2018.09.02

View this article at: <http://dx.doi.org/10.21037/ales.2018.09.02>

We are grateful to Dr. Beppu and colleagues for their insightful comments on our recent study. Laparoscopic liver resection (LLR) for colorectal liver metastases (CRLM) has been widely diffused with the accumulation of evidence of its safety and feasibility. Additionally, several studies have elucidated the operative advantages of LLR for CRLM including less intraoperative blood loss and shorter postoperative hospital stay (1-3). In the current study, we demonstrated the oncologic advantage of LLR for patients with CRLM. The propensity score-based analysis enabled to compare well-matched 22 LLR and 44 open liver resection (OLR) patients with CRLM, and then showed that LLR allows to initiate adjuvant chemotherapy (AC) significantly earlier than OLR (4).

Although this study has several limitations, we would like to respond to the comments raised by Dr. Beppu and colleagues. In our study, well-matched LLR and OLR groups showed similar postoperative outcome including Clavien-Dindo grades (5) and postoperative hospital stay. Additional analysis revealed that the frequency of simultaneous resection of primary colorectal cancer was also comparable (1/22 case in LLR group and 1/44 case in OLR group, $P=1.000$). As for the preference of the surgeon in determining AC initiation, there was no significant difference in surgeons performing liver resection between two groups ($P=0.345$). Although the logistic regression multivariate analysis on factors associated with AC delay was difficult in our study due to the patient number, these additional results reinforce that the impact of LLR on the timing of AC initiation may be independent from

postoperative complications.

For the reasons why LLR enables to shorten the duration between operation and the start of AC, we hypothesized that less surgical trauma due to LLR may accelerate the rehabilitation of patients with CRLM, and thus may contribute to initiate AC within appropriate timing. As suggested by Dr. Beppu and colleagues, health-related quality of life (HRQOL) assessed by the 36-item Medical Outcomes Study Short Form test has been used as an objective evaluation of postoperative recovery. In the Oslo laparoscopic versus open liver resection for colorectal metastases (OSLO-COMET) randomized controlled trial (RCT), demonstrating surgical advantages of LLR with solid evidence, showed significantly higher HRQOL in LLR than OLR group (6). However, since the duration between liver resection and AC initiation was not examined in this RCT, the influence of better HRQOL on the timing of AC has not been revealed. In our propensity score-based retrospective study, the underlying mechanism of the quicker return to AC in LLR group was also unclear due to the lack of information regarding postoperative objective assessments such as HRQOL in CRLM patients underwent LLR or OLR.

The significance of AC after liver resection for patients with CRLM has been confirmed in various studies (7-9). Currently a randomized phase II/III trial comparing liver resection followed by mFOLFOX6 with liver resection alone as treatment for CRLM (JCOG0603) is underway (10). Together with the results of our present study, LLR and the delivery of AC without delay have been becoming the standard

treatments for patients with CRLM. Future prospective multi-institutional studies will demonstrate the oncologic advantage of LLR for CRLM including early recovery-based AC with appropriate timing and excellent long-term survival. Once again, we appreciate the valuable comments provided by Dr. Beppu and colleagues.

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.2018.09.02>). 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.2018.09.02

Cite this article as: Kawai T, Scatton O. Adjuvant chemotherapy without delay, an oncologic advantage of laparoscopic liver resection for colorectal liver metastases. *Ann Laparosc Endosc Surg* 2018;3:73.