Editorial

Win ratio approach to compare laparoscopic with open liver resection for colorectal cancer liver metastases

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Colorectal cancer is the leading cause of cancer-related death globally. The liver is the most predominant site for metastatic disease. Approximately 20–30% of patients diagnosed with colorectal cancer develop liver metastases. Surgical resection is considered the only potentially curative treatment for colorectal liver metastases (CRLM) (1). Several studies have indicated that liver resection provides favorable long-term survival for patients with CRLM. Both open liver resection (OLR) and laparoscopic liver resection (LLR) are used to treat CRLM, and the incidence of LLR has been increasing. LLR is a minimally invasive technique that has become predominantly used for treating CRLM. The first international consensus conference in Louisville in 2008 recommended LLR for solitary tumors measuring ≤5 cm in the anterolateral segments (2). The second international consensus conference in Morioka established minor LLR as a standard procedure (3). Recently, short-term outcomes have demonstrated that LLR leads to lower morbidity, less blood losses, fewer transfusions, and shorter hospital stays compared to OLR. The first randomized trial, OSLO-COMET, showed a shorter hospital stay and lower morbidity in the LLR group compared with the OLR group (4). More recently, the Southampton Consensus Guidelines for laparoscopic liver surgery recommended LLR for CRLM as a valid alternative to OLR, based on superior short-term outcomes and non-inferior oncologic and survival outcomes. These guidelines also indicated that large tumors (>5 cm in size) and lesions located close to major vessels can be addressed with LLR without increased morbidity in expert hands (5). The recently published LapOpHuva study, a second prospective randomized controlled trial comparing LLR and OLR, also demonstrated that LLR resulted in a lower morbidity rate (6). Meanwhile, the adequacy of resection margin status and long-term outcomes remain major concerns for oncologic results, as the loss of tactile feedback prevents palpation of solid lesions within the liver parenchyma during LLR. However, the OSLO-COMET prospective trial revealed no difference in the R0 resection rate or positive resection margin rate between the LLR and OLR groups. The LapOpHuva randomized trial used a secondary endpoint to compare long-term outcomes, which were similar between LLR and OLR groups. A meta-analysis of propensity-matched studies that included 2,259 patients revealed that LLR was associated with better 3-year overall survival, though this difference was not sustained at 5 years (7). Similarly, a recent meta-analysis of individual patient data from two randomized trials and 13 propensity-matched studies demonstrated that LLR exhibited superior survival rates for CRLM, even at the 10-year mark, particularly in elderly patients (8). Therefore, while there is no consensus on the superiority of LLR for both short- and long-term outcomes, several studies have indicated its benefits.

Pocock *et al.* (9) first proposed the win ratio approach in a 2012 article in the *European Heart Journal*, which was later applied in cardiology trials (10). Clinical trials frequently use

composite endpoints analyzed with time-to-event statistical methods, such as Cox proportional hazards regression. A limitation of these methods is that all composite outcomes are treated as equivalent, and the first component to occur is the one that contributes. Win ratios have been introduced to address this limitation, as they prioritize the results within a composite outcome according to a predefined hierarchy. Additionally, win ratios enable the inclusion of different types of endpoints (e.g., time-to-event, categorical, or continuous) within one composite, allowing each endpoint to be analyzed independently. Recognizing that even a single result can affect the direction of the win rate, statistical significance is crucial. When evaluating composite results, the effect of individual factors on the impact of an intervention must be considered. Additionally, the inclusion and order of outcomes within the hierarchy require careful attention.

Paro *et al.* (11) analyzed an international cohort of 962 patients from five centers to evaluate the overall benefit of LLR for CRLM compared to OLR using the win ratio. Patients were paired and matched according to age, lesion number and size, lymph node status, and preoperative chemotherapy receipt. The outcomes were evaluated in a hierarchical order: 90-day mortality, complication severity, time to death, time to recurrence, and margin status. The study revealed a 1.77 win ratio in favor of LLR. Furthermore, the win ratio favored LLR regardless of tumor burden, unilobar or bilobar disease, and tumor location within the liver. The win ratios were particularly pronounced for short-term outcomes, including 90-day mortality and complication severity. This finding indicates a composite clinical benefit of LLR with the win ratio approach for short- and long-term outcomes. This study made a significant contribution to the literature on the clinical benefit of LLR for CRLM compared with that of OLR. The current findings clarify the expected benefits of LLR, providing important information for surgeons when selecting LLR for CRLM.

However, the study by Paro *et al.* has several limitations that should be noted. First, it was a retrospective study, and bias in selecting LLR or OLR could not be fully excluded, despite matching patient characteristics. Second, the number of patients undergoing LLR was relatively small. Third, the long study period may have influenced the results, as medical techniques and treatment selection have evolved over time. Finally, the learning curve could not be evaluated because the study was conducted across multiple centers. However, the participating centers specialized in both open and laparoscopic hepatobiliary surgeries, and the multi-institutional nature of the analysis improves the generalizability of the results to other centers.

The results of this study based on the win ratio approach will be validated at other facilities, and the composite clinical benefit of LLR for CRLM will be further clarified. Such further verification will strengthen the robustness of the findings.

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Footnote

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References

1. Kabir T, Syn N, Goh BKP. Current status of laparoscopic liver resection for the management of colorectal liver metastases. J Gastrointest Oncol 2020;11:526-39.
2. Buell JF, Cherqui D, Geller DA, et al. The international position on laparoscopic liver surgery: The Louisville

Statement, 2008. Ann Surg 2009;250:825-30.
3. Wakabayashi G, Cherqui D, Geller DA, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg 2015;261:619-29.
4. Fretland ÅA, Dagenborg VJ, Bjørnelv GMW, et al. Laparoscopic Versus Open Resection for Colorectal Liver Metastases: The OSLO-COMET Randomized Controlled Trial. Ann Surg 2018;267:199-207.
5. Abu Hilal M, Aldrighetti L, Dagher I, et al. The Southampton Consensus Guidelines for Laparoscopic Liver Surgery: From Indication to Implementation. Ann Surg 2018;268:11-8.
6. Robles-Campos R, Lopez-Lopez V, Brusadin R, et al. Open versus minimally invasive liver surgery for colorectal liver metastases (LapOpHuva): a prospective randomized controlled trial. Surg Endosc 2019;33:3926-36.
7. Zhang XL, Liu RF, Zhang D, et al. Laparoscopic versus open liver resection for colorectal liver metastases: A systematic review and meta-analysis of studies with propensity score-based analysis. Int J Surg 2017;44:191-203.
8. Syn NL, Kabir T, Koh YX, et al. Survival Advantage of Laparoscopic Versus Open Resection For Colorectal Liver Metastases: A Meta-analysis of Individual Patient Data From Randomized Trials and Propensity-score Matched Studies. Ann Surg 2020;272:253-65.
9. Pocock SJ, Ariti CA, Collier TJ, et al. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. Eur Heart J 2012;33:176-82.
10. Ferreira JP, Jhund PS, Duarte K, et al. Use of the Win Ratio in Cardiovascular Trials. JACC Heart Fail 2020;8:441-50.
11. Paro A, Hyer JM, Avery BS, et al. Using the win ratio to compare laparoscopic versus open liver resection for colorectal cancer liver metastases. Hepatobiliary Surg Nutr 2023;12:692-703.

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