Editorial Commentary

Minimally invasive hepatectomy is here to stay, but more evidence is needed

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Comment on: Zhu P, Liao W, Zhang WG, *et al*. A prospective study using propensity score matching to compare long-term survival outcomes after robotic-assisted, laparoscopic, or open liver resection for patients with BCLC stage 0-A hepatocellular carcinoma. Ann Surg 2023;277:e103-11.

Keywords: Minimally invasive hepatectomy (MIH); laparoscopic hepatectomy; robotic hepatectomy

Submitted Jun 23, 2023. Accepted for publication Jul 03, 2023. Published online Jul 04, 2023.
doi: 10.21037/hbsn-23-309
View this article at: https://dx.doi.org/10.21037/hbsn-23-309

In their recent study, "*A prospective study using propensity score matching to compare long-term survival outcomes after robotic-assisted, laparoscopic, or open liver resection for patients with BCLC stage 0-A hepatocellular carcinoma*", Zhu *et al.* established three prospective cohorts of patients with Barcelona Clinic Liver Cancer (BCLC) stage 0–A hepatocellular carcinoma (HCC) who underwent curative open liver resection (OLR), laparoscopic liver resection (LLR), or robot-assisted liver resection (RALR) at a single institution. In this study, all participating surgeons had passed the learning curves for LLR and RALR and were experienced in OLR. Short- and long-term oncologic outcomes of these approaches were examined using propensity score matching to account for the different distribution of covariates among the three groups. The main findings were that laparoscopic and robotic approaches resulted in longer operative times and duration of Pringle's maneuver compared to open surgery. However, there were no differences in 5-year disease-free or overall survival. In a multivariate Cox regression model, the authors demonstrate that clinically significant portal hypertension, elevated alpha-fetoprotein (AFP), and Edmondson-Steiner grading (III + IV) were independent risk factors for long-term survival. The conclusions from this study demonstrate the safety and effectiveness of both robotic and laparoscopic hepatectomies in patients with BCLC stage 0–A HCC in comparison to open hepatectomy (1). The authors point to the fact that both laparoscopic and robotic liver resections have become commonplace, but the evidence to support their use, especially in long-term oncologic outcomes, is not robust, calling for more rigorous evaluation of surgical innovation.

An innovative procedure in surgery has been described as, "*a new or modified surgical procedure that differs from currently accepted local practice, the outcomes of which have not been described, and which may entail risk to the patient*" (2). Surgeons are both natural and trained innovators, performing daily situational assessment, analyzing decisions, and improvising in each patient-specific clinical case to provide creative solutions to the challenges of surgical practice (2,3). In addition to this, the development context of innovation is important—with a litany of historical examples of how innovations have been dismissed by the medical and surgical community at one time point and later broadly accepted (3). In contrast to the rigorous process used for the testing and introduction of new pharmacological interventions, many major surgical innovations, such as laparoscopic cholecystectomy, have been pursued in the name of improving the health of individual patients and then published as non-comparative trials (2). While laparoscopic cholecystectomy has become commonplace, it is not without potential harm. Attempts have been made to establish frameworks for surgical innovation that consider patient protection from harm at the forefront (4). One factor that differentiates surgical innovation from innovation in the pharmaceutical arena is the presence of a surgeon's own learning curve (5).

The surgeon's learning curve has been a specific limitation to the widespread adoption of laparoscopic and robotic hepatectomy. There are well known limitations of minimally invasive surgery (MIS) include restriction of manipulation, loss of manual palpation and reduced global vision. Since the introduction of laparoscopic liver resection in the 1990's, quickly followed by the introduction of robotic liver resection, many studies have been published examining the learning curve for minimally invasive hepatectomy (MIH) and attempting to define the magic number of procedures a surgeon would need to perform to be proficient. The learning curve for a surgeon is influenced by many factors other than the specific procedure at hand, for example, their overall skill level, their prior experience with open hepatectomy and MIS more generally, the quality of assistant available to them and institutional experience. A recently published systematic review and meta-analysis included 40 studies related to learning curves in MIH. Using cumulative summative methodology, the median overall number of procedures required for LLR was found to be 50 (range, 25–58) and for RALR was 25 (range, 16–50). Interestingly, they also identified that there was a year-on-year reduction in the number of procedures needed to become proficient at MIH—with 48.3 cases in 1995 and 19.9 cases in 2020. The learning curve also varied based on type of hepatectomy performed, with 53 (range, 44–60) for major hepatectomy and 24 (range, 16–58) for minor hepatectomy. Most of the studies included evaluated institutional learning curves rather than single surgeon learning curves (6).

In addition, establishing the safety and efficacy of new innovations is critical to maintain patient safety and ensure optimal patient outcomes. There are several guidelines that support the use of LLR including the Morioka Guidelines, published in 2015, which contended that at that time LLR for minor hepatectomy had become standard practice, while LLR for major hepatectomy was still an innovative procedure in the exploration phase. All of the evidence available was of low quality and they called for higher quality evaluative studies (7). The Asia Pacific Consensus Statement on LLR for HCC was published in 2018 and asserted that laparoscopic minor hepatectomy, particularly left lateral sectionectomy was a preferred practice for HCC at experienced centers. They also contended that laparoscopic major hepatectomy is a challenging procedure and should only be performed at centers of excellence (8). Recently, guidelines on how to safely perform MIH have also been published (9).

Importantly, there continues to be accumulating evidence regarding long term oncologic outcomes for MIH in cancer surgery. The OSLO-COMET trial, a randomized trial data to support the use of laparoscopic liver resection for colorectal liver metastases was published in 2018. This study compared parenchymal sparing LLR to OLR. LLR group experienced less 30-day complications (19% *vs.* 31%, P=0.021) and had shorter hospital stays (53 *vs.* 96 hours, P<0.001). There were no differences in operative blood loss, operation time or resection margins (10). A small randomized controlled trial compared LLR *vs.* OLR for solitary HCCs <5 cm and demonstrated that LLR had shorter operative time, shorter hospital stay, and comparable complications with similar R0 resections and disease-free and overall survival (11). The AP-LAPO trial is an on-going international, multicenter, randomized trial of laparoscopic *vs.* open major hepatectomy for HCC which will test the hypothesis that laparoscopic major hepatectomy is associated with less tumor recurrence and better survival compared with open major hepatectomy (12).

Zhu *et al.* conducted a well-designed single institution prospective study comparing minimally invasive techniques to open approaches for resection of early HCC. Although the findings provide further evidence that minimally invasive techniques for cancer may have similar long term oncologic outcomes compared to open resection, the authors acknowledge that more robust evaluation is needed as the study was not randomized and was significantly limited by patient selection, with each individual surgeon determining the surgical approach. In summary, more rigorous prospective and randomized trials comparing open *vs.* laparoscopic *vs.* robotic hepatectomy should be conducted to guide physicians in counseling their patients and making decisions regarding operative approach. Additionally, published guidelines should be updated to reflect current experience, data and practice.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Hepatobiliary Surgery and Nutrition*.

The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-309/coif). AT serves as an unpaid Editorial Board Member of *Hepatobiliary Surgery and Nutrition*. The other author has 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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Cite this article as: Beal EW, Tsung A. Minimally invasive hepatectomy is here to stay, but more evidence is needed. HepatoBiliary Surg Nutr 2023;12(4):619-621. doi: 10.21037/hbsn-23-309