



Modern surgical approach to hepatocellular carcinoma

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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.

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We are glad to contribute with an editorial on the important topic of therapeutic opportunities for hepatocellular carcinoma (HCC). The increasing diffusion of minimally invasive approaches to the liver and the growing experience worldwide have progressively changed our curative strategies for patients affected by primary and metastatic liver tumors (1). The pillars of this evolution in the field of surgical treatment for liver neoplasms are technical, anatomical and physiological. From a technical standpoint, minimally invasive approaches to the liver have switched the visualization of the organ from the anterior to the caudal view (2), modifying the resection planes, the transection technique and the vascular control. This is closely linked to the anatomical aspect of the innovation: in fact, thanks to the magnified vision and the different surgical perspective, novel techniques like Glissonian pedicle-based resections are currently spreading as part of a parenchyma-sparing concept. Lastly, we reached a deeper knowledge of liver function with specific regard to the future liver remnant (FLR) after major liver resection, including the functional reserve of cirrhotic patients and the role of portal pressure, affecting post-operative outcomes and risk of post-hepatectomy liver failure. In other words, the attention is currently mostly focused on the remaining liver rather than on the disease to treat. Consistently, the latest Barcelona Clinic Liver Cancer (BCLC) staging system update in

2022 opened to a comprehensive evaluation of the liver function, including the role of portal hypertension and functionality of the FLR in the therapeutic algorithm (3). Minimally invasive surgery, either laparoscopic or robotic, has a relevant role in this specific setting thanks to the preservation of porto-systemic shunts, reduction of liver decompensation and lower impact on the abdominal wall (4).

Zhu and colleagues recently reported a prospective study with propensity score matched (PSM) analysis comparing patients that underwent either minimally invasive (laparoscopic and robotic) or open liver resection in patients affected by HCC stage 0–A according to BCLC (5). In an 18-month interval, 369 HCC patients were enrolled and after PSM, 168 patients were matched, accounting for 56 patients in each group. Patients aged 14 to 75 years, with no history of other malignant diseases, and no previous treatment for HCC before liver resection were included. It is interesting to mention that the choice of the surgical technique (open or minimally invasive) was based on the patient’s wish after discussion with the operating surgeon. Short-term results confirmed the trend in literature of slightly but significantly longer operative time in the minimally invasive groups compared to open surgery, nonetheless post-operative stay was significantly shorter in the robotic and laparoscopic group. Of note, 5 patients in the robotic group were converted to open due

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to uncontrollable bleeding in three cases, intraoperative tumor rupture in one case, and inability to proceed the last one. Regarding oncological accuracy of the minimally invasive approach, Authors reported 5-year overall survival (OS) rates of 78.6%, 76.8%, and 74.4% for open liver resection (OLR), laparoscopic liver resection (LLR), and robot-assisted liver resection (RALR), respectively, and 5-year disease-free survival (DFS) rates of 57.9%, 51.3%, and 51.8%, respectively, with no statistically significant differences. Interestingly, they reported that tumor diameter (≥ 5 cm), clinically significant portal hypertension (CSPH), α -fetoprotein (AFP) level (≥ 400 ng/mL), and Edmondson-Steiner grading (III + IV) have a negative effect on 5-year OS on univariate analysis, while CSPH, AFP level > 400 ng/mL and tumor grading are independent risk factors of poor long-term survival. Actually, this is consistent with the observations coming from the field of liver transplantation, showing that biological criteria as AFP fluctuations, response to locoregional treatments and tumor grading can accurately predict the risk of recurrence (6).

This study confirms the importance of expanding the indications to laparoscopic and robotic approaches, that convey not only the well-known advantages of minimally invasive surgery, but also equal oncological success and potential advantages in patients with CSPH. Nonetheless we believe that the need for randomized controlled trials can be actually mitigated since the evidence on the safety and efficacy of minimally invasive liver resections are so solid that we cannot ethically consider an open resection whenever a minimally invasive approach is available. The use of difficulty scales may help centers to stratify the procedures according to the proficiency of each surgeon in the team, in order to offer to all patients the best outcome possible (7). We are nowadays experiencing a growth of laparoscopic and robotic experience worldwide, leading to more and more complex cases performed with a minimally invasive approach, including donor hepatectomy, reconstructive surgery, and liver transplantation as well (8-10). Moreover, robotic surgery proved his effectiveness also as a bridging strategy in patients candidate to liver transplantation, compared to other strategies (11,12). HCC presents with specific challenges due to the natural history of the disease and the frequent association with liver cirrhosis. Both Eastern and Western series have demonstrated the non-inferiority of robotic approach compared to open controls in terms of both short- and long-term outcomes (13,14). Thanks to those evidence is now clear that robotic and laparoscopic resections for HCC

are as safe as the standard open approach when performed in expert and high volume centers, where surgeons completed the learning curve of both open and minimally invasive procedures. The community of hepato-pancreato-biliary (HPB) surgeons should contribute to a collective effort to offer patients the best treatment, improving surgical education programs and referring patients to high volume centers.

Given the equipoise of the technical approaches, it remains the issues of indication, timing and benefit between liver resection and liver transplantation under the light of modern transplant oncology conception (15). A tumor biology-guided approach should be pursued including a multidimensional evaluation of each case, balancing all the available strategies, including advanced downstaging with combined surgery, radiology and check-point inhibitors agents, and considering living donation as a valuable tool to match the perfect timing for liver transplantation.

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