Peer Review File

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Reviewer A

Comment 1: Table 1: P-values in several categorical variables seem to be incorrect, such as Intraoperative complications, morbidity, conversion, etc. Furthermore, as Satava grade I complication rates seem to be comparable between the groups, the superiority of RoboLap approach in terms of Satava grade I complications is not appropriate.

Reply 1: Thank you for your thorough review and valuable feedback on the statistical analysis and Table 1 of our manuscript. We sincerely appreciate the time and effort you have dedicated to assessing our work.

In response to your concerns regarding Table 1 and the p-values for various categorical variables, we have carefully reviewed the statistical analysis with the assistance of a professional statistician. As a result, we have ensured the accuracy of the p-values associated with each categorical variable.

Regarding the Satava complications, we have now included p-values for each grade (I to III) to provide a comprehensive view of the statistical significance. Upon this reevaluation, we found a significant difference in Satava grade III intraoperative complications between the two approaches. Specifically, the Robotic group exhibited higher rates of Satava grade III complications compared to the RoboLap group (2 (7.1%) vs 0 (0.0%); $p = 0.029$). According to our modified results, we agree that the RoboLap approach offers benefits not for low-grade Satava but for high Satava intraoperative grade. Table 1 and the Results section have been modified accordingly.

Changes in the Text 1: "The groups were found to be comparable in terms of patient characteristics and liver disease burden. While the two groups showed similar intraoperative bleeding, periprocedural transfusion rates, conversion rates, and complications, the Robo-Lap group demonstrated a reduction in parenchymal transection time (170 ± 65 vs. 248 ± 51 min; $p = 0.025$), a decrease in the risk of Satava grade III complications (0 (0.0%) vs. 2 (7.1%); $p = 0.029$) [5], and a reduction in the use of sutures to repair vascular and/or small biliary damages during the parenchymal transection phase (13 (46.4%) vs. 3 (4.6%); $p < 0.001$) (Table 1). In the robotic group,

sutures were utilized in 7 cases to repair minor defects in secondary or tertiary biliary branches, and in 1 case to address a minor injury to adjacent organs. The remaining cases involved the use of sutures to repair small tangential vascular breaches. Conversely, in the Robo-Lap group, only 2 cases necessitated sutures for vascular repair. A decrease in the need for hemostatic agents for temporary and definitive hemostasis was also reported (19 (67.9%) vs. 25 (38.5%); p = 0.009). When considering the achievement of optimal intraoperative outcomes, the probability of uneventful surgery for technically complex resections was more frequent in the RoboLap group than in the pure Robotic group."

Changes in Table 1: Please reference file attached.

Comment 2: Lines 63-67: This interpretation is inappropriate, because the rates of conversion, blood transfusion and R0 resection were comparable between the groups.

Reply 2: Thank you for your valuable feedback. We appreciate your observation regarding lines 63-67. We agree that the interpretation provided in those lines was not appropriate, given the comparable rates of conversion, blood transfusion, and R0 resection between the groups.

We have thoroughly revised the "Results" section of the manuscript in line with the comments provided, including those related to the statistical analysis (see Comment 1). As a result, the mentioned sentence has been removed to ensure an appropriate interpretation of the results.

Changes in the Text 2: Please reference Comment 1 and the revision of Table 1.

Comment 3: The rate of vascular damages that need suturing in pure robotic approach was too high. What were the reasons for such high rate? What did the surgeons use for parenchymal dissection in pure robotic approach? Both groups used Pringle maneuver in approximately 100% of cases, and so the operative field seemed to be dry enough for surgeons to safely identify vascular structures and dissect the parenchyma.

Reply 3: Thank you for your insightful comment regarding the rate of vascular damages and the need for suturing in our pure robotic approach for minimally invasive liver resections. We appreciate the opportunity to provide additional context and clarification on this matter.

In our study, a total of 93 technically complex minimally invasive liver resections were performed, encompassing both the pure robotic and Robo-Lap approaches. The overall requirement for sutures during parenchymal transection was calculated to be 16 out of the 93 cases (17.2%), broken down into 13 cases for the pure robotic group and 3 cases for the Robo-Lap approach. It's important to note that the utilization of sutures was not limited solely to repairing vascular damages. The robotic platform's dexterity facilitates the execution of intracorporeal sutures with greater ease and precision. Consequently, even for minor biliary defects in secondary or tertiary branches, which could potentially have been managed using fibrin sealant patches, a small suture was preferred to ensure meticulous closure. Sutures were also used in case of small damages to adherent or adjacent organs. Additionally, we compared our suturing rates to a study by Halls[1], focusing on intraoperative complications during laparoscopic liver resections. Halls reported a comparable rate of 18.9% for intraoperative complications in a cohort exceeding 2000 laparoscopic liver resections, which included not only high Iwate complexity resections but also a wide spectrum of resection's complexity.

1. Halls MC, Berardi G, Cipriani F, Barkhatov L, Lainas P, Harris S, D'Hondt M, Rotellar F, Dagher I, Aldrighetti L, Troisi RI, Edwin B, Abu Hilal M. Development and validation of a difficulty score to predict intraoperative complications during laparoscopic liver resection. Br J Surg. 2018 Aug;105(9):1182-1191. doi: 10.1002/bjs.10821. Epub 2018 May 8. PMID: 29737513.

In reference to the technique utilized for parenchymal transection in the pure robotic approach, the branches of bipolar forceps were used to execute a Kellyclasia-like dissection technique. This involved a clamp-crushing approach where mechanical parenchymal demolition was achieved by crushing hepatocytes with Kelly forceps. The objective was to split hepatocytes while safeguarding vascular (portal and hepatic veins) and biliary structures, subsequently coagulating or closing them between clips based on their size.

Change in the Text 3: ***Introduction section***: "In the pure robotic approach, the branches of bipolar forceps were employed in a Kellyclasia-like fashion to revisit the clamp-crush technique for parenchymal transection. Vascular and biliary structures were sealed or closed between clips, according to the caliber."

Results section: "The groups were found to be comparable in terms of patient characteristics and liver disease burden. While the two groups showed similar intraoperative bleeding, periprocedural transfusion rates, conversion rates, and complications, the Robo-Lap group demonstrated a reduction in parenchymal transection time (170 ± 65 vs. 248 ± 51 min; $p = 0.025$), a decrease in the risk of Satava grade III complications (0 (0.0%)

vs. 2 (7.1%); p = 0.029) [5], and a reduction in the use of sutures to repair vascular and/or small biliary damages during the parenchymal transection phase (13 (46.4%) vs. 3 (4.6%); p < 0.001) (Table 1). In the robotic group, sutures were utilized in 7 cases to repair minor defects in secondary or tertiary biliary branches, and in 1 case to address a minor injury to adjacent organs. The remaining cases involved the use of sutures to repair small tangential vascular breaches. Conversely, in the Robo-Lap group, only 2 cases necessitated sutures for vascular repair. A decrease in the need for hemostatic agents for temporary and definitive hemostasis was also reported (19 (67.9%) vs. 25 (38.5%); p = 0.009). When considering the achievement of optimal intraoperative outcomes, the probability of uneventful surgery for technically complex resections was more frequent in the RoboLap group than in the pure Robotic group."

Comment 4: The authors should compare RoboLap and pure Laparoscopic approaches and assess the merits or demerits of using the robotic platform at your institution.

Reply 4: Thank you for your valuable suggestion regarding comparing the RoboLap and pure Laparoscopic approaches and evaluating the merits and demerits of using the robotic platform at our institution.

We appreciate your insightful recommendation. However, we would like to highlight that our institution boasts nearly two decades of extensive experience in laparoscopic liver surgery, establishing us as a tertiary high volume referral center, performing over 50 laparoscopic liver resections annually. Given this rich background, a direct comparison between the highly standardized laparoscopic approach, which has been refined over the years, and the relatively recent Robo-Lap approach initiated in 2022, might inadvertently introduce a bias towards the laparoscopic approach, potentially yielding skewed results favoring its outcomes.

In order to maintain a fair and unbiased comparison, we believe it would be more informative to contrast the Robo-Lap approach with groups or institutions that have less experience in laparoscopic liver surgery. This comparison would provide a more accurate assessment of the potential advantages and limitations of the Robo-Lap technique, showcasing its unique contributions and advancements in the field.

We genuinely appreciate your suggestion and agree that this comparison is a topic worthy of a comprehensive and original manuscript rather than a viewpoint. We are committed to further exploring this concept and are considering it for a dedicated research study to offer a more in-depth analysis.

Comment 5: The indications included a significant number of cholangiocarcinoma and preoperative biliary drainage was performed in 15-20% of cases. Are these cases perihilar cholangiocarcinoma and did these require bilio-enteric anastomosis? If so, it would not be appropriate to include these cases in this study, because the techniques and expected perioperative outcomes would be very different between simple hepatectomy and hepatectomy with biliary reconstruction.

Reply 5: Thank you for bringing this crucial point to our attention. We appreciate your insight and acknowledge the importance of maintaining homogeneity in the study population, particularly concerning the surgical techniques, and expected perioperative outcomes associated with major liver resection and biliary reconstruction for perihilar cholangiocarcinoma. Even though preoperative biliary drainage is a routine part of our preoperative optimization protocol, performed not only for perihilar cholangiocarcinoma but also for various other diagnoses involving malignant biliary obstruction, we concur with your assessment.

In response to your concern, we have meticulously reviewed and refined our study, now excluding all cases of perihilar cholangiocarcinoma from the viewpoint.

Change in Text 5: ***Methods Section:*** "All cases of perihilar cholangiocarcinoma were intentionally excluded due to the distinct surgical techniques applied and expected perioperative outcomes."

Changes in Table 1: Please reference file attached.

Reviewer B

Comment 1: The paper would benefit from a thorough revision for language to improve readability as it contains multiple syntax and grammatical errors.

Reply 1: Thank you for your comment. In response to your suggestion, we have conducted a comprehensive review of the manuscript, specifically focusing on language improvement and syntax correction to enhance readability. The revisions were overseen by a native speaker to ensure accuracy and fluency in the text.

Comment 2: A diagram to demonstrate where they place their ports, especially the bedside surgeon's trocar relative to the robotic trocars, would be informative.

Reply 2: Thank you for the suggestion. We have incorporated a diagram illustrating the placement of the ports, particularly highlighting the location of the bedside surgeon's trocar in relation to the robotic trocars.

Change in Text 2: ***Methods section:*** "A diagram illustrating port placement, emphasizing the location of the laparoscopic trocar relative to the robotic trocars is shown in Figure 2."

Please Reference Figure 2. Also reported below.

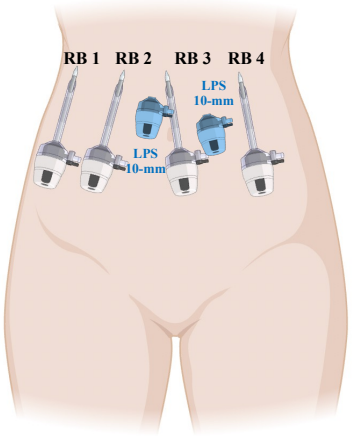

Figure 2: The Da Vinci X platform was utilized for all procedures. The first surgeon operated the console, assisted by the bed-side surgeon positioned between the patient's legs. A 10-mm laparoscopic trocar was inserted infraumbilically in a right pararectal position to create pneumoperitoneum (LPS 10-mm). Four robotic trocars were placed in a standardized configuration: one on the right flank (RB 1), one along the mid-clavicular line (RB 2), one in the midline (RB 3), and one in the left hypochondrium (RB 4). The robotic platform was docked and positioned in a reverse-Trendelenburg stance. A second laparoscopic access was added following the docking of robotic arms. This was done to prevent any potential interference between laparoscopic and robotic instruments and to enhance ergonomic efficiency. Standard robotic instruments were used, including prograsp forceps, Maryland bipolar forceps or long bipolar forceps, monopolar scissors, and a robotic clip applier. A camera was positioned on arm 2 (mid-clavicular line) to ensure the line of transection was in view of both the first surgeon and the assistant.

Comment 3: Is it possible that the greater transection time, as well as the greater rate of bleeding and use of hemostatic agents, had to do with a cumulative effect of elements including a greater rate of cirrhosis (HCC represented 38% of the robot cohort, and 20% of the robo-lap cohort), more numerous tumors, more extensive or complex hepatectomies, etc, in the pure robotic cohort? I think the authors need to acknowledge the limitations of their retrospective single-institution data a bit more.

Reply 3: Thank you for your insightful comment regarding potential cumulative effects and for the time spent in reviewing our manuscript. We appreciate the opportunity to address these concerns and acknowledge the limitations of our study.

In our analysis, we observed no statistically significant differences in patient characteristics and liver disease burden between the pure Robotic and Robo-Lap groups. Both groups exhibited similar intraoperative bleeding, periprocedural transfusion rates, conversion rates, and overall complications. The only statistically significant differences were noted in the reduction of parenchymal transection time, fewer Satava grade III complications, decreased use of intraoperative sutures, and a reduction in the use of hemostatic agents in the Robo-Lap group compared to the pure Robotic group.

Regarding the differing percentages of hepatocellular carcinoma (HCC) representation in the two groups, we acknowledge that this variation may be attributed to the relatively small sample sizes within each group. We concur with your suggestion that this aspect should be explicitly mentioned in the limitations section of our study to ensure transparency and a comprehensive understanding of the data.

Changes in Text 1: ***Limitations Section:*** "Given the retrospective design and the limited patient cohort, interpreting the findings is influenced by these limitations. Future multi-institutional studies, involving tertiary centers with extensive experience in minimally invasive liver surgery techniques, are crucial to better evaluate the potential benefits of the Robo-Lap approach."

Comment 4: In addition, for purely robotic cases, who serves as the bedside assist? Is it possible that the advantages seen with the combo approach are due to the presence of TWO skilled surgeons who might give each other advice to avoid trouble compared to ONE attending/skilled surgeon and a bedside assist who might be less experienced (e.g. trainee or nurse or surgical tech)?

Reply 4: Thank you for highlighting an essential aspect regarding the role of the bedside assistant in our study, particularly focusing on their expertise and consistency across both approaches. In our study, we maintained consistency by having the same highly experienced junior attending physician serve as the bedside assistant for both purely robotic cases and the Robo-Lap cases. This approach ensured that a skilled and proficient surgeon, well-versed in minimally-invasive techniques, provided valuable assistance throughout the procedures. In both scenarios, whether for purely robotic cases or Robo-Lap cases, the bedside assistant's expertise was a vital component contributing to the overall success of the surgery. This involved employing a mixed transection technique during Robo-Lap cases, combining laparoscopic ultrasonic dissector manipulation by the bedside surgeon with actions performed by the primary surgeon at the console utilizing robotic monopolar scissors and bipolar forceps.

Changes in Text 4: ***Methods Section:*** "In all cases, a highly experienced junior attending physician, skilled in minimally invasive techniques, served as the bedside assistant for both purely robotic and Robo-Lap procedures, ensuring consistent expertise and support throughout."

Comment 5: Given your single-institution experience, I would recommend tempering the interpretation of your findings, especially in your conclusions. Perhaps add something like "in our hands" to the final sentence.

Reply 5: We completely agree with your perspective and have revised our conclusion to appropriately reflect our single-institution experience.

Changes in Text 5: ***Conclusion section:*** "In conclusion, the Robo-Lap approach for complex anatomical resections has the potential to enhance intraoperative outcomes by optimizing the execution of an uneventful parenchymal transection phase."

Reviewer C

Comment 1: This is a Viewpoint describing techniques of combined laparoscopic and robotic-assisted hepatectomy. This technique has been described by multiple other authors and is sometimes referred to as Roboscopic. Please consider referencing some previously published manuscripts, here are some examples :

Roboscopic minimally invasive pancreaticoduodenectomy: mixing laparoscopic and robotic approach in order to achieve better postoperative outcomes September 2021HPB 23:S1013DOI:10.1016/j.hpb.2021.08.758 Conference: 14th Congress of the European-African Hepato-Pancreato-Biliary Association (E-AHPBA), 15-17 September 2021, Bilbao. Virtual Congress

Perrakis A, Rahimli M, Gumbs AA, Negrini V, Andric M, Stockheim J, Wex C, Lorenz E, Arend J, Franz M, Croner RS. Three-Device (3D) Technique for Liver Parenchyma Dissection in Robotic Liver Surgery. J Clin Med. 2021 Nov 12;10(22):5265. doi: 10.3390/jcm10225265. PMID: 34830547; PMCID: PMC8653962. Rahimli Mirhasan; Aristotelis Perrakis; Vera Schellerer; Andrew Gumbs; Eric Lorenz; Mareike Franz; Jörg Arend; Victor-Radu Negrini; Roland Siegfried Croner. Robotic and laparoscopic liver surgery for colorectal liver metastases: an experience from a German Academic Center. World Journal of Surgical Oncology. 2020 Dec 22;18(1):333. doi: 10.1186/s12957-020-02113-1. PMID: 33353551; PMCID: PMC7756910. Gumbs AA, Lorenz E, Tsai TJ, Starker L, Flanagan J, Benedetti Cacciaguerra A, Yu NJ, Bajul M, Chouillard E, Croner R, Abu Hilal M. Study: International Multicentric Minimally Invasive Liver Resection for Colorectal Liver Metastases (SIMMILR-CRLM).

Cancers (Basel). 2022 Mar 8;14(6):1379. doi: 10.3390/cancers14061379. PMID: 35326532; PMCID: PMC8946765.

Reply 1: Thank you for your valuable suggestion regarding referencing previously published manuscripts related to the described technique, sometimes referred to as Roboscopic. We appreciate your recommendation, and we have now included the relevant references in the manuscript.

Change in Text 1: See reference # 4.

Comment 2: I believe a more comprehensive definition of robotic-assisted surgery would improve the manuscript. Many authors have come to the realization that current complete surgical robotic systems are merely telemanipulators and are not true robots. Please consider some of the arguments in this paper to enhance your discussion.

Andrew A. Gumbs, Mohammad Abu-Hilal, Tzu-Jung Tsai, Lee Starker, Elie Chouillard, Roland Croner. Keeping surgeons in the loop: are handheld robotics the best path towards more autonomous actions? (A comparison of complete vs. handheld robotic hepatectomy for colorectal liver metastases). Artificial Intelligence Surgery. 2021

Reply 2: Thank you for your valuable input. We appreciate your suggestion regarding a more comprehensive definition of robotic-assisted surgery. We acknowledge that there is an ongoing discussion within the scientific community regarding the classification of current surgical robotic systems as telemanipulators rather than true robots. We carefully consider the arguments presented in the referenced paper to enhance and refine our discussion on this topic. We also acknowledge the concept of "Handled Robotics" as described by Gumbs et al., which highlights the importance of maintaining haptics in robotic procedures.

The Robo-Lap approach, as mentioned, can indeed be considered a form of "Handled Robotics" with the unique advantage of preserving haptics while integrating the benefits of the CUSA. We believe that this approach has the potential to serve as a platform for rapid learning and skill development, ultimately leading towards autonomous actions guided by the operating surgeon. Ultimately, we envision a progression towards a pure robotic approach, wherein the robotic system itself is trained to perceive and utilize haptic feedback, further advancing the field of robotic surgery. The suggested reference has been added to the “Bibliography” section.

Changes in the Text 2: ***Discussion Section:*** "The determination of the superior robotic approach in liver resection surgery requires further investigation, especially as more surgical centers gain expertise in robotic techniques. The Robo-Lap approach aligns with Gumbs et al. concept of "Handled Robotics",[8] combining the preservation of haptics while retaining the benefits of the Cavitron Ultrasonic Surgical Aspirator (CUSA). Additionally, it stands as a valuable platform for rapid skill acquisition, enabling the development of autonomous actions guided by the operating surgeon. This evolutionary pathway holds promise for the progression towards a fully autonomous robotic approach, where the robotic system is trained to interpret and utilize haptic feedback efficiently."

Comment 3: Lastly, recent studies have focused on how experience influences outcomes. I believe a comment on how much laparoscopic and robotic assistance the surgeons had before embarking on this approach would be useful. Were the surgeons first laparoscopic trained, or did they go from open surgery directly to robotic surgery. Lastly, are any of the surgeons formally trained in minimally invasive surgery? Andrew A Gumbs, Mohamed Abu Hilal, Roland Croner, Brice Gayet, Elie Chouillard, Michel Gagner. The initiation, standardization and proficiency (ISP) phases of the learning curve for minimally invasive liver resection: comparison of a fellowship-trained surgeon with the pioneers and early adopters. Surg Endosc. 2020 Nov 10. doi: 10.1007/s00464-020-08122-1

Reply 3: Thank you for your comment. We appreciate your interest in the surgeons' experience and training in laparoscopic and robotic assistance. These aspects are now comprehensively addressed in the methods section of our manuscript, where we provide detailed information about the surgeons' training and experience in both laparoscopic and robotic procedures.

Change in the text 3*: Methods Section:* "All resections were performed after the 25th case of the overall series of robotic resections by three senior surgeons, each with extensive experience in both open and minimally invasive liver hepatectomies and having received a full training both as console and table surgeons. All minimally invasive resections were performed at IRCCS San Raffaele Hospital, Milan. The center, originally established as a high-volume laparoscopic center (conducting more than 50 laparoscopic liver resections per year), smoothly transitioned to incorporating the robotic approach into daily practice.

In all cases, a highly experienced junior attending physician, skilled in minimally invasive techniques, served as the bedside assistant for both purely robotic and Robo-Lap procedures, ensuring consistent expertise and support throughout."

Editorial Comments:

Comment 1: The editorial board believed that statistical analyses and the interpretation of the results were not satisfied and it may need to be improved. The rate of vascular damage in robotic approach seems to be rather high, the authors need to explained.

Reply 1: Thank you for your feedback. We appreciate your concern regarding the statistical analyses and result interpretation. We have taken these concerns seriously and thoroughly reevaluated all the points raised. The issues have been carefully addressed and rectified, with comprehensive discussions presented in response to ***Reviewer A Comment 1 and Reviewer A Comment 3***. We believe the revised manuscript now provides a more robust and insightful interpretation of the results, including a thorough exploration of the rate of vascular damage associated with the robotic approach. We apologize for any inconsistencies that may have been present in the initial submission and appreciate the opportunity to enhance the clarity and rigor of our manuscript.