

Response to: “Comment on: Prognostic Effect of Liver Resection in Extended Cholecystectomy for T2 Gallbladder Cancer Revisited: A Retrospective Cohort Study with Propensity-Score-Matched Analysis”

Yeshong Park, MD,* Jun Suh Lee, MD, PhD,* Boram Lee, MD,* Yeongsoo Jo, MD,* Eunhye Lee, MD,* MeeYoung Kang, MD,* Wooil Kwon, MD, PhD,† Chang-Sup Lim, MD, PhD,‡ Jin-Young Jang, MD, PhD,† Ho-Seong Han, MD, PhD* and Yoo-Seok Yoon, MD, PhD,*

We appreciate the interest of Dr. Zhang and colleagues in our multicenter study evaluating the prognostic effect of liver resection during extended cholecystectomy for T2 gallbladder cancer.¹

The first issue raised by the authors relates to the standard surgical practice for T2 gallbladder cancer at the participating centers. During the study period, cholecystectomy with liver resection was performed in a total of 8 patients, while 19 patients at Seoul National University Bundang Hospital received cholecystectomy only. Considering that 329 patients underwent extended cholecystectomy including lymph node dissection (LND) with or without liver resection, the proportion of patients receiving only cholecystectomy or cholecystectomy with liver resection was small. This indicates that LND with or without liver resection was the standard surgical practice for T2 gallbladder cancer at all participating centers.

The second issue relates to the quality of propensity score matching (PSM). In our original study, PSM was conducted for age, sex, operation method, T stage, lymph node metastasis, and adjuvant treatment. After matching, all factors except the operation method were well-balanced, with a standard mean difference less than 0.2. However, regarding the operation method, there was a significant difference in the initial study population: while 74.1% of patients in the LND with liver resection (LND+L) group underwent open surgery, 92.0% of the surgical procedures in the LND only (LND) group were performed using minimally invasive techniques. Consequently, matching for the operation method reduced the sample size to approximately 30 patients in each group, and the variable remained unbalanced with even wider calibers. As a reduction in sample size could limit the

credibility of the results, we decided to perform full matching, including all patients in the initial LND group. As a result, the standard mean difference for the operation method was larger than 0.2 in the final matched analysis, which we acknowledged as a limitation in the original article. However, even considering the relatively large variability in the operation method, the C-statistic for the established PSM model was 0.855.

The authors further pointed out that the difference in operative methods between the 2 groups could have influenced operative parameters and short-term postoperative outcomes. However, the primary focus of our study was to assess the impact of liver resection on long-term oncologic outcomes including recurrence and cancer-related death. We found that there were no significant differences in disease-free survival and overall survival between the LND+L and LND groups. Multivariable regression analyses revealed that the operative method (open *vs* laparoscopic/robotic) was not a prognostic factor for recurrence or cancer-related death. These results were in accordance with previous studies comparing open and laparoscopic extended cholecystectomy, which found no statistically significant difference in long-term outcomes between the 2 groups.²⁻⁴

We agree with Dr. Zhang and colleagues on the limitations of our study, including its retrospective design and small sample size. However, due to the rarity of gallbladder cancer and the advanced stage at which most patients are diagnosed, the incidence rate of T2 stage tumors is quite low. Therefore, we believe that our original study, which included 197 patients from 3 tertiary referral centers, provides valuable information from which meaningful conclusions about oncological outcomes can be drawn. These results may serve as a basis for designing future prospective studies. It is important to note that there was missing data in preoperative serum carcinoembryonic antigen and carbohydrate antigen 19-9 levels, as well as pathologic information including histologic differentiation, angiolymphatic invasion, and venous invasion. Missing data were removed and not included in the analysis.

From the *Department of Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam-si, Korea; †Department of Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; and ‡Department of Surgery, Seoul National University Boramae Medical Center, Seoul National University College of Medicine, Seoul, Korea.

Reprints: Yoo-Seok Yoon, MD, PhD, Department of Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82, Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, 13620, Republic of Korea. E-mail: yoonys@snuh.org.

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Surgery Open (2023) 4:e352

Received: 21 September 2023; Accepted 25 September 2023

Published online 3 November 2023

DOI: 10.1097/AS9.0000000000000352

REFERENCES

1. Park Y, Lee JS, Lee B, et al. Prognostic effect of liver resection in extended cholecystectomy for T2 gallbladder cancer revisited: a retrospective cohort study with propensity-score-matched analysis [published online ahead of print]. *Ann Surg*. 2023. doi:10.1097/SLA.0000000000005908.
2. Agarwal AK, Javed A, Kalayarasan R, et al. Minimally invasive versus the conventional open surgical approach of a radical cholecystectomy for gallbladder cancer: A retrospective comparative study. *HPB (Oxford)*. 2015;17:536–541.
3. Yoon YS, Han HS, Cho JY, et al. Is laparoscopy contraindicated for gallbladder cancer? A 10-year prospective cohort study. *J Am Coll Surg*. 2015;221:847–853.
4. Itano O, Oshima G, Minagawa T, et al. Novel strategy for laparoscopic treatment of pT2 gallbladder carcinoma. *Surg Endosc*. 2015;29:3600–3607.