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LETTER – HEPATOBILIARY TUMORS

Response to: "Surgical Volume Alone Does Not Determine Outcome Following Liver Transplant for Perihilar Cholangiocarcinoma"

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To the Editor

We appreciate the comments of Hand et al. [1] in regard to our recent study demonstrating that center experience affects post-liver transplant outcomes in patients with hilar cholangiocarcinoma (Ph-CCA).

Hand et al. [1] pointed out wide variation in volume among well-experienced centers. We agree that well-experienced centers had a large variety of case numbers based on our definition (six or more cases between 2010 and 2017) in our study and therefore compared post-transplant outcomes between the largest center, other well-experienced centers, and less-experienced centers (fewer than six cases between 2010 and 2017) to mitigate the effect of wide variation in case volume.[2] When comparing post-transplant outcomes between the largest center and the rest of the centers in our cohort, the largest center showed a relatively better 3- and 5-year patient survival and lower mortality due to recurrence, but the difference was not significant. However, in this comparison, the impact of center experience may be diluted. As shown in Fig. 3 in our article, there was a significant difference in outcomes between the largest center and the less-experienced center group, and the risk was comparable between the largest center and other well-experienced centers. The discrepancy of liver transplant outcomes found in our study should be recognized.

With regard to the recent meta-analysis involving 20 studies of unresectable Ph-CCA that demonstrated similar survival rates between the Mayo Clinic and other centers,[3] a possible explanation for the discrepancy of these results (5-year patient survival in non-Mayo centers: Cambridge et al. 60.6% vs. our study 33.0%) is that the meta-analysis might underestimate the impact of center experience since the literature was selected based on the quality and number of cases included in each study, which might miss outcomes in transplant centers that did not have enough experience to be reported. This may cause selection bias. Our study investigated all transplant centers in the US and could capture the entire experience and nationwide outcomes of liver transplant for CCA in the US. Given the relatively small number of cases in each transplant center, the retrospective cohort study using a national transplant registry should more accurately reflect actual practice than the meta-analysis.

We do not consider that surgical experience itself determines post-transplant outcomes. Treatment strategies for CCA require a multidisciplinary approach. While current requirements for model for end-stage liver disease (MELD) exception score includes neoadjuvant therapy followed by a staging laparotomy,[4] it is unclear whether accurate diagnosis based on staging laparotomy has been uniformly performed among all transplant centers in the US. Center experience may affect the quality of preoperative management, including diagnostic imaging studies,

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pretransplant neoadjuvant therapy, and staging laparotomy. Therefore, appropriate patient selection and assessment might not be well achieved in the less-experienced centers. Although we acknowledge that multiple factors such as different decision-making processes or unit structures between centers might affect outcomes following liver transplantation,[5] our findings emphasize the importance of uniform patient selection and pretransplant neoadjuvant therapy protocol among transplant centers to achieve successful outcomes.

We acknowledge that the Organ Procurement and Transplantation Network and United Network for Organ Sharing (OPTN/UNOS) registry does not include detailed information regarding oncological status and pretransplant treatment history, which is one of the limitations of our study. As future directions, we proposed that detailed pretransplant treatment history and explant pathology should be reported and monitored by OPTN/UNOS to improve indication criteria and to determine appropriate policy for the exception for Ph-CCA. The association between center experience and oncological findings at the time of transplant should be assessed in future studies.

We appreciate the comments made by Hand et al. [1] and welcome further insight into the effect of center experience on outcomes after liver transplantation in patients with Ph-CCA.

DISCLOSURE Toshihiro Kitajima, Tayseer Shamaa, Taizo Hibi, Dilip Moonka, Gonzalo Sapisochin, Marwan S. Abouljoud, and Shunji Nagai have no conflicts of interest to declare as defined by *Annals of Surgical Oncology*.

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