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Editorial

Achieving Sufficient Therapeutic Outcomes of Surgery in Elderly Hepatocellular Carcinoma Patients through Appropriate Selection

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See "Efficacy and Safety of Surgical Resection in Elderly Patients with Hepatocellular Carcinoma: A Systematic Review and Meta-Analysis" by Jin-Soo Lee, et al. on page 695, Vol. 18, No. 4, 2024

Despite a decrease in the overall incidence of hepatocellular carcinoma (HCC) in South Korea from 2008 to 2018, the age-standardized incidence of HCC among elderly individuals has continued to rise.[1] Projections indicate that the crude incidence of HCC among the elderly will increase, accounting 21.3% of the total HCC population by 2028. Despite the substantial increase in HCC disease burden among elderly individuals, there is still considerable debate about the most appropriate treatment options for managing this patient population. Major factors complicating treatment decisions include the underrepresentation of elderly patients in clinical trials, concerns related to coexisting comorbidities, frailty, and decreased liver function.[2]

Several studies investigating the feasibility and safety of various treatment modalities in elderly patients with HCC have demonstrated that advanced age is not a contraindication for HCC treatment.[3,4] Among treatments for HCC, surgical resection is an invasive procedure associated with higher comorbidities and surgical risks. Therefore, in elderly patients, the procedure is greatly influenced by the patient's characteristics, leading to concerns about its effectiveness and safety. The study conducted by Lee *et al.*[5] suggests that with careful selection of surgical candidates, the efficacy outcomes of surgical resection in elderly HCC patients are not worse than those in non-elderly patients. The authors aimed to provide systematic evidence on the efficacy and safety outcomes of surgical resection in elderly HCC patients with a meta-analysis of 56 studies.

The study found that the efficacy outcomes of surgical resection in elderly patients were not significantly different from those in non-elderly patients. The overall survival hazard ratio of elderly was only 1.26 (95% confidence interval [CI], 0.92 to 1.74), and the disease-free survival hazard ratio was 1.03 (95% CI, 0.99 to 1.08). However, the risk of mortality was higher in the elderly group defined as ≥75 years compared to the non-elderly group, largely due to lower heterogeneity in studies using 75 as the age threshold. This highlights the need for a common definition of elderly across diverse clinical settings, particularly recognizing that in the elderly, specifically those aged 75 and older or even the "super elderly" aged 80 and older, the survival benefits from surgery may be lower compared to non-elderly patients.[5]

Regarding safety, the elderly group exhibited higher postoperative mortality rates, particularly in the 30-day, 90-day, and in-hospital periods. The overall complication incidence was also higher in the elderly group with an odds ratio of 1.44 (95% CI, 1.22 to 1.69). While the elderly group is at a higher risk for surgical complications or mortality, the overall survival benefit from surgery was similar between the elderly and non-elderly groups. However, patients with a higher risk of postoperative complications or mortality, especially those with significant cardiovascular comorbidities or impaired liver function, require careful consideration when deciding on surgical intervention.

A recent study conducted by our research group found lower rates of surgery in elderly patients compared to non-elderly patients across Barcelona Clinic Liver Cancer (BCLC) stages: 13.9% versus 25.6% for BCLC stage 0, 26.3% versus 43.0% for BCLC stage A, and 11.0% versus 15.7% for BCLC stage B, using data from the Korean Pri-

mary Liver Cancer Registry.[3] However, inverse probability of treatment weighting analysis showed that overall survival was similar between elderly and non-elderly patients in both early and intermediate stages. Importantly, overall survival was significantly better in elderly patients who received treatment compared to those who did not (median, 38.6 months vs 22.3 months; p<0.001). Therefore, while comparing outcomes of elderly and non-elderly patients is clinically meaningful, it is crucial to consider that appropriate treatment can improve clinical outcomes even in elderly patients. This underscores the importance of considering active treatment strategies regardless of age, which can potentially enhance patient outcomes.

Although the study of Lee *et al.*[5] demonstrates significant clinical implications, several limitations should be noted. First, the majority of studies (83.9%) were conducted in Asia, with only a small proportion (16.0%) from Europe, potentially limiting the generalizability of findings to other regions. Indeed, the study observed less pronounced differences in the overall survival and disease-free survival between elderly and non-elderly groups in Asia compared to non-Asian regions. Regional differences are crucial in HCC research, owing to disparities in etiology of liver disease and surgical practices between these areas. Second, all 56 studies were retrospective cohort studies, which may introduce biases and limit the ability to establish causal relationships. Third, variability in defining elderly patients: 42.8% of studies used an age threshold of 70 years, while others used thresholds of 75 years (25%) and 65 years (8.9%), which may affect the comparability and interpretation of results across studies.

The advancement in surgical techniques and postoperative management has likely contributed to improved surgical outcomes in elderly patients with HCC. Therefore, in the current era of increasing elderly HCC patients, surgical resection should be actively considered as a treatment option as their overall survival and disease-free survival are comparable to those of non-elderly patients. However, the higher rates of postoperative mortality and complications necessitate thorough postoperative care and extended in-hospital monitoring, especially for the super elderly. Future studies should focus on adjusting for comorbidities and surgical methods to better understand the variables affecting efficacy and safety outcomes. In addition, developing a scoring system or guideline to assist in the decision-making process for surgical treatment in elderly HCC patients is essential for optimizing clinical outcomes.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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