



Letter to the Editor

Comment on: Influence of Recipient Age on Outcomes After Liver Transplantation for Hepatocellular Carcinoma

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Dear Editor,

Any individual above the age of 65 years is defined as elderly, and it has been shown that major abdominal operations carry a high risk of morbidity and mortality when compared to patients of younger age.

Hepatocellular carcinoma (HCC) is the 6th most common cancer in both sexes and the 4th leading cause of cancer-related deaths.^[1,2] HCC usually develops on a cirrhotic background, and therefore, liver transplantation (LT) is the only therapeutic modality that has the potential to cure both diseases simultaneously.^[2] Diagnosis, treatment, and the course of HCC in the elderly are challenging. For this reason, we read the article by Gonultas et al.^[3] with great interest. The authors analyzed 535 patients who underwent LT for HCC between April 2006 and March 2025, including 68 patients aged 65 years or older. Their data demonstrate a significant increase in elderly recipients over the last five years, rising from 2.5% (2002–2010) to 9.4% (2021–2025, $p < 0.001$). Among HCC cases specifically, the proportion of elderly patients increased from 6.3% to 17.5% ($p = 0.039$) over the same period.

While the survival rates in the elderly group were acceptable, they were significantly lower than those of their younger counterparts, with a mean overall survival of 2497.5 days versus 3793.5 days, respectively ($p = 0.012$). The 1-, 5-, and 10-year survival rates for the elderly (81.5%, 52.8%, and 39.7%) were also significantly lower than those of younger patients.

A critical finding in the data provided by Gonultas et al.^[3] is that 60% ($n = 41$) of the elderly patients were beyond the Milan criteria. Of these, 28 patients (68% of advanced cases) exceeded the Malatya criteria, and 26 (63%) exceeded the Expanded Malatya criteria. Notably, 32% of these cases had a total tumor diameter exceeding 8 cm. Although the authors did not provide a specific analysis of these advanced cases—specifically regarding exact tumor diameters—the results remain acceptable despite the advanced stage of the disease. The inclusion of these advanced tumors may stem from the fact that these classifications were based on final pathology rather than pre-transplant imaging. Furthermore, the higher rate of patients beyond the Milan criteria in the elderly group may suggest a delay in diagnosis within this age group.

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The study also highlights the utility of the Malatya criteria, which incorporated an additional 13 patients beyond the Milan criteria (a ~25% expansion). In contrast, only two patients (7% of those beyond the Malatya criteria) met the Expanded Malatya criteria. In the younger cohort, 219 patients (46.9%) were beyond Milan; of these, 52 (24%) fell within the Malatya criteria and 27 (17%) within the Expanded Malatya criteria.

While these findings might suggest a difference in tumor biology or stage at diagnosis, the authors found no significant differences in AFP levels or tumor differentiation between the age groups, which argues against a distinct biological divergence. Recurrence rates were also similar, though the younger group showed higher hepatic recurrence, while the elderly showed more frequent distant metastasis. A notable limitation of the study is the lack of data regarding locoregional therapy (LRT) and subsequent response rates. Such information would have provided valuable insight into the biological behavior of HCC across these two age groups. The authors have found age to be a factor increasing the risk of mortality, and their results are supported by previous studies.^[4]

Nevertheless, the treatment of HCC in patients is not governed by age. However, the outcome of LT in elderly patients has contradictory results.^[5-8] Selection of elderly patients for liver transplantation should be individualized, as there are no clear selection criteria in this age group.^[8] Frailty is a very important factor when treating elderly individuals. Frailty can be defined as the presence of chronic systemic diseases and nutritional deficiencies that significantly compromise the outcomes of surgery and other systemic treatments. This is particularly evident in oncological cases and major procedures such as liver transplantation.^[9,10] There is not much that can be done for frail elderly patients other than offering the best supportive care.^[4] It has been shown that in early-stage HCC, various treatment modalities such as local ablation or transarterial chemoembolization (TACE) resulted in comparable outcomes in elderly and non-elderly patients. Furthermore, in intermediate-stage tumors, surgery or TACE resulted in similar overall survival in both elderly and non-elderly patients.^[11]

There are various differences in HCC in the elderly when compared to adolescents and young adults. Older patients are more likely to have Hepatitis C (HCV) infection or Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) (formerly NASH). In contrast, Hepatitis B (HBV) is less common in this age group.^[12] Tumors in the elderly are frequently well-differentiated and may exhibit less aggressive biological behavior. They are more likely to emerge as single nodules rather than multinodular diseases. High rates of concurrent conditions such as diabetes, hyperten-

sion, and cardiovascular disease are common, which often complicate the treatment decisions. In adolescents and young adults, tumor biology is more aggressive.^[12] On the other hand, the diagnosis of HCC with routine surveillance is harder in elderly patients.

Conclusion

In conclusion, the treatment of HCC requires a multidisciplinary and individualized approach, and this is especially true for elderly patients. While the majority of them are frail and best supportive care may be required, some may benefit from multimodal treatment, including liver transplantation or major hepatic resections.

Disclosures

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