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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Liver Transplantation for Hepatocellular Carcinoma

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PAST

It is controversial if living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) offer similar outcomes for hepatocellular carcinoma (HCC). Studies that compared the outcomes of LDLT and DDLT for HCC drew contradictory conclusions. LDLT and DDLT are different in terms of graft availability, allocation, waiting time, need for bridging therapy, risk of dropout, surgical technique, and graft size. The potential concerns of LDLT for HCC include a fast tracking effect and the possibility of higher tumor recurrence after transplant.[1] The caveat is that survival data were evaluated from the time of transplant rather than from the time of listing, therefore the effect of waiting time and dropout was not considered. Another key issue is that LDLT patients tend to have more advanced tumor stage and have more salvage transplant. There were two reports from the French centers that evaluated outcomes of HCC patients from the time of listing but did not demonstrate any survival difference.[2,3]

PRESENT

Given the deceased organ shortage, it was not surprising to observe a significant survival benefit for HCC after LDLT with intention-to-treat (ITT) analysis in our study.[4] Overall, 375 HCC patients were listed for transplant (188 ITT-LDLT and 187 ITT-DDLT). The dropout rate was lower in the ITT-LDLT group (14.4 vs. 57%; $p < 0.001$), and the 1-, 3-, and 5-year overall survival rates were significantly better in the ITT-LDLT group than the ITT-DDLT group (94.1 vs. 77.5%, 81.4 vs. 48.7%, and 75.9 vs. 40.8%; $p < 0.001$). A total of 246 patients reached transplant (LDLT, $n = 161$; DDLT, $n = 85$), and LDLT patients were younger, had more advanced tumors, and had a higher pretransplant α-fetoprotein (AFP) level. Propensity score matching was used to control for differences in clinicopathological characteristics. The 1-, 3-, and 5-year overall survival (95.4 vs. 98.5%, 80.0 vs. 92.3%, and 73.4 vs. 84.4%; $p = 0.146$) and recurrence-free survival (87.7 vs. 90.8%%, 76.9 vs. 83.1%, and 72.2 vs. 81.5%; $p = 0.246$) rates were comparable between the matched LDLT and DDLT groups.

FUTURE

A well-designed, randomized trial will be ideal to investigate whether LDLT and DDLT are equivalent for HCC patients, but this is ethically unacceptable. The two approaches should be viewed as complementary rather than mutually exclusive. The success of liver transplant depends on our ability to predict and prevent tumor recurrence. Currently, most transplant criteria are based on anatomical variables (tumor size, tumor number, tumor volume, etc.) and surrogate markers of tumor aggressiveness (differentiation, tumor grade, lymphovascular invasion, AFP, etc.). Unfortunately, tumor recurrence is likely multifactorial and a reliable biomarker is lacking. Whether a living donor

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partial graft sustains more ischemic/reperfusion injury, and the rapidly regenerating graft might in turn stimulate tumor growth and recurrence, remains unknown. There is increasing evidence to show that tumor inflammatory microenvironment and early-phase graft injury might be related to tumor recurrence.[5] Taken together, a reliable biomarker that allows us to predict tumor recurrence and attenuate graft injury will be important.

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