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Invited Commentary

Improving patient selection in Living-Donor Liver transplantation: Prognostication with pre-transplant 18-fluoro-deoxyglucose Positron Emission Tomography

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Invited commentary for IJS-D-19-00151R2 "FDG-PET predicted unfavorable tumor histology in Living Donor Liver transplant recipients; a retrospective cohort study"

The decisive cure for Hepatocellular Carcinoma (HCC) and its underlying causative disease is a Liver Transplantation (LT) [1]. Given the sparsity of available grafts for donation, Living-Donor Liver Transplantation (LDLT) has become an important option in treatment algorithms for HCC. However, this has met skepticism due to a higher incidence of recurrence when compared to alternative Deceased-Donor Liver Transplantation (DDLT) [1–3]. It is thought that the "regeneration effect" of the transplanted graft, more prominent in LDLT than in DDLT, could support remnant cancer cell growth, especially in a suppressed immunosurveillance state. Not surprisingly, tumors with a propensity for microvascular invasion (mVI) and higher replication rates such as poorly differentiated HCC, sarcomatous HCC, combined Hepatocellular Cholangiocarcinoma and Intrahepatic/Hilar Cholangiocarcinoma tend to do poorly with LDLT and have been proposed to be an exclusion criteria for LT [2].

The Milan / University of California San Francisco (UCSF) / Pittsburg / Tokyo / Kyoto criterion are widely used by high volume centers for candidacy consideration in HCC, and rely heavily on tumor size/number and relation to vascular structures based on imaging [4]. Nevertheless, they lack specificity in determining above-mentioned unfavorable biology characteristics. A complementary pathologic diagnosis could fill this gap. However, the fears of seeding the biopsy tract with malignant cells or obtaining false negative results constrain this practice. Thus, new tools that can offer a better insight in tumor biology are being developed.

In this current edition of International Journal of Surgery, Leong-Liung Ling et al. [5] report the possible prognostication value of ^{18}-fluoro-deoxyglucose Positron Emission Tomography (FDG-PET) prior to LT. In a retrospective study of 258 patients, authors found that a tumor/non-tumor ratio (TNR) of 1.3 or higher [calculated by standardized-uptake values sampled at the highest activity of any tumor region of interest (ROI) (SUV_{max}) over the average of three regions of interest (ROIs) within normal liver parenchyma (SUV_{mean})]; was statistically associated (61.5% vs. 13.5% $p < 0.001$) and highly specific (86.5%) with tumors with unfavorable biology in the resected specimen. Positivity on FDG-PET was also associated with mVI. Importantly, multivariate analysis showed that positive FDG-PET, mVI and unfavorable histology were all strong independent predictors for recurrence impacting overall survival after transplant. Interestingly, the cross-table subgroup analyses showed that FDG-PET-negativity had lower recurrence rates (0% vs. 8.9%, $p = 0.636$) regardless of their histologic result (favorable vs. unfavorable), whereas FDG-PET-positivity in spite of having a favorable histology had a 30.3% rate of recurrence, challenging this particular histopathologic paradigm. Not surprisingly, patients with FDG-PET-positivity and unfavorable tumor histology had the worst outcome with 87.5% recurrence rate. Changing the TNR cutoff value to 2.0 improved sensitivity, specificity, and other test performance values, indicating a need for further optimization in a prospective clinical trial, that would define better its place in pretransplant evaluation. Considering the possible health, psychological and socio-economical risks for donors and the impossible to ignore risk of performing a futile operation, transplant physicians have an ethical responsibility to select the most ideal candidates. This study although limited by its single center nature and small number of patients is a right move in this direction.

Provenance and peer review

Invited commentary, internally reviewed.

References

[1] L.M. Kulik, R.A. Fisher, D.R. Rodrigo, R.S. Brown Jr., C.E. Freise, A. Shaked, et al., Outcomes of living and deceased donor liver transplant recipients with hepatocellular carcinoma: results of the A2ALL cohort, Am. J. Transplant. 12 (11) (2012) 2997–3007.

[2] M.S. Park, K.W. Lee, H. Kim, Y.R. Choi, G. Hong, N.J. Yi, et al., Primary living-donor liver transplantation is not the optimal treatment choice in patients with early hepatocellular carcinoma with poor tumor biology, Transplant. Proc. 49 (5) (2017) 1103–1108.

[3] S. Abu-Gazala, K.M. Olthoff, Status of adult living donor liver transplantation in the United States: results from the adult-to-adult living donor liver transplantation

https://doi.org/10.1016/j.ijsu.2019.10.038
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cohort study, Gastroenterol. Clin. N. Am. 47 (2) (2018) 297–311.
[4] S.K. Hong, K.W. Lee, H.S. Kim, K.C. Yoon, N.J. Yi, K.S. Suh, Living donor liver transplantation for hepatocellular carcinoma in Seoul National University, Hepatobiliary Surg. Nutr. 5 (6) (2016) 453–460.
[5] L.L. Ling, C.C. Hsu, C.C. Yong, A.M. Elsarawy, Y.C. Chan, C.C. Wang, W.F. Li, T.L. Lin, F.Y. Kuo, Y.F. Cheng, L.M. Lin, C.L. Chen, C.C. Lin, FDG-PET predicted unfavorable tumor histology in living donor liver transplant recipients; a retrospective cohort study, Int J Surg 69 (2019) 124–131.

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