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The use of HCV positive donors among non-HCV infected liver transplant recipients

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Liver transplantation (LT) is a life-saving procedure and in some cases, the only mode of management. It is an ideal form of treatment in conditions like end-stage liver disease, acute liver failure and hepatocellular carcinoma within specific criteria. Unfortunately, the liver transplant demand continues to exceed donor liver supply, this alarming disparity has resulted in a high waiting-list death rate. In a 2019 study (Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients, OPTN/SRTR), 52.2% of adult patients had to wait for more than 1 year for a liver transplantation.[1] A simultaneous increase in opioid-related deaths in the United States has left the organ procurement system with the increasing availability of young, hepatitis C virus (HCV) nucleic acid testing (NAT) positive donors, and they are estimated to contribute, if they are used, 300 to 500 additional liver grafts to the liver donor pool.[2] Obviously, these HCV-positive donors can be easily used among HCV recipients, if the recipient has not been treated pre-LT. Our initial experience has revealed higher mortality associated with pre-LT treated patients compared with pre-LT untreated patients. A 3.9 times higher 12 months mortality risk was seen for a pre-LT-treated group compared to a pre-LT-untreated group, providing a survival advantage in deferring post-transplant therapy period.[3] This is thought to be due to the fact that pre-LT recipients treated with direct acting anti-viral drugs (DAA's) did not have access to younger HCV-positive grafts. Our thinking about holding off the pre-LT HCV treatment has changed with the first report of successful treatment of HCV in a pre-LT HCV-treated recipient who received HCV-positive younger graft due to the urgency of transplantation, due to Hepato-Pulmonary Syndrome.[4]

The expected concern with the use of HCV positive grafts to HCV RNA negative recipients is the deliberate transmission of infection and its consequences. Therefore, the goal is to tackle the soaring LT waiting-list mortality by putting these HCV-positive grafts into use in such a way that the transmission of the donor infection is controlled/treated, and transplant outcomes are similar to that of an HCV negative donor.[5]

In 2013, the United States Public Health Service proposed updated guidelines for reducing the transfer of human immunodeficiency virus, hepatitis B virus, and HCV virus through organ transplantation.[6] Application of these guidelines, along with the use of well- tolerated, pan-genotypic direct antiviral drugs (DAA's) could provide a controlled environment in which HCV-infected donor livers could be safely used in HCV-negative recipients. As for the credibility of the direct-acting antiviral drugs (DAA's), they are proven to be effective in eliminating HCV infection from more than 95% of the allografts.[7] The sustained virologic response is said to occur when HCV RNA is no longer detectable after 12 weeks of DAA therapy and this corresponds with a decreased liver morbidity and mortality.[8,9] The timing for commencement of post-transplant DAA's should ideally be as soon as possible to prevent graft complications, like fibrosing cholestatic hepatitis.[10] The type and duration of DAA therapy after LT depend on the genotype of the virus received from the donor.[11] HCV positive donors to HCV positive recipient LT using DAAs is a common practice and has led to a spike in the use of similar donors for uninfected recipients as well. A study conducted in 2021 showed a 35-fold increase in LT of HCV positive donors to HCV negative recipients in the last 4 years in the United States, increasing from 8 in 2016 to 280 in 2019.[12] Another study showed how DAA resulted in a threefold increase in LT from HCV positive to HCV negative recipients from 2015 to 2016.[13] This trend is supported by numerous studies with favorable outcomes for this strategy. A study carried out in 2018 at Stanford showed acceptable short-term outcomes for using HCV-positive donor grafts in 10 non-infected recipients.[14] All 10 non-infected recipients in the study received post-transplant donor HCV infection and each successfully achieved sustained virologic response after 12 weeks of direct antiviral drug therapy.[14] No graft loss or deaths were reported during a 380-day post-transplant follow-up period and as a result, the study emphasized the use of HCV-positive donor grafts to expand the LT donor pool.[14] A retrospective study conducted at Johns Hopkins Hospital examined 26 HCV seronegative patients who had received liver grafts from HCV seropositive donors between January 1, 2017, to August 31, 2019, resulted in good short-term outcomes for HCV cure following DAA's.[11] In 2021, Cotter et.al reported no discernible impact on medium-term outcomes and excellent grafts survivals from HCV-infected donor to uninfected recipient LT. The 1-year graft survival rates were 91% and 90%- and 2-year rates were 88.5% and 87% for HCV infected donor to HCV negative recipient and uninfected donor to uninfected recipient, respectively (p=0.672).[12] In another study, a single-centre retrospective analysis of LT performed on HCV seronegative recipients from HCV seropositive organs showed equal post-transplant complication rates between NAT-positive and NAT-negative recipients.[15] The study concluded that HCV seropositive organs could be safely used in HCV

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seronegative patients with minimal post-transplant complications.[15] One concern in LT from HCV positive donor to HCV negative recipient is the increased risk of fibrosis progression in post-transplant. A pre-DAA multi- center, European study conducted in 2011 compared graft and survival outcomes of LT among 63 HCV-positive donor and 63 HCV-negative donor recipients, but the fibrosis stage in the donor graft was not more than stage 1.[16] The study ended up reporting no statistical differences in their outcomes.[16] Another study proposed an algorithm in which liver biopsy on HCV NAT-positive donor was suggested, and grafts greater than stage 2 fibrosis were discarded.[17] Thus, if a pre-transplant biopsy is performed for NAT-positive donors and grafts with fibrosis above a pre-determined cut-off are filtered, the risk of fibrosis as a post-transplant complication can be minimized. Owing to the DAA's, HCV can be treated rather than merely controlled, thus, more studies are needed in favor of using HCV-positive donor grafts for HCV-negative recipients. This has led to the exploration of other barriers which could affect this type of transplantation, such as accessibility, cost and tolerance of DAA's. A single-center, retrospective study done by Edmonds et al.[18] analysed access to DAA's, time to first dose post-transplant, and cost of DAA's. They found that the median time from transplant to first dose was 45 days, and that the co-pay assistance program reduced the median monthly patient cost from 1914 $ to 0 $, and concluded that although DAA's were affordable, brisk administrative efforts to speed up insurance approval and providing co-pay assistance were required.[18] Therefore, even though we have excellent anti-HCV regimens in hand, it is also important to pay enough attention to sound health policies to improve DAA access.

In conclusion, given the high waiting-list mortality in LT, the use of HCV-positive donor livers for HCV-negative recipients is an attractive option. With the excellent efficacy and good transplant outcomes of DAA in multiple studies, this strategy makes much more sense. Meanwhile, there is a current need for sound healthcare policies which will ensure the effective implementation of this strategy, not only in the US, but all over the world.

References

1. Kwong AJ, Kim WR, Lake JR, Smith JM, Schladt DP, Skeans MA, et al. OPTN/SRTR 2019 Annual Data Report: Liver. Am J Transplant 2021;21(Suppl 2):208-315.
2. Goldberg DS, Blumberg E, McCauley M, Abt P, Levine M. Improving organ utilization to help overcome the tragedies of the opioid epidemic. Am J Transplant 2016;16(10):2836-2841.
3. Strauss AT, Ishaque T, Weeks S, Hamilton JP, Simsek C, Durand CM, et al. Pretransplant Hepatitis C virus treatment decreases access to high-quality Livers. Transplant Direct 2021;7(4):e684.
4. Saberi B, Hamilton JP, Durand CM, Li Z, Philosophe B, Cameron AM, et al. Utilization of hepatitis C virus RNA-positive donor liver for transplant to hepatitis C virus RNA-negative recipient. Liver Transpl 2018;24(1):140-143.
5. Muhammad H, Zaffar D, Tehreem A, Ting P-S, Simsek C, Turan İ, et al. An update on usage of high-risk donors in liver transplantation. J Clin Med 2022;11(1):215.
6. Seem DL, Lee I, Umscheid CA, Kuehnert MJ. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep 2013;128(4):247-343.
7. Kwo PY, Mantry PS, Coakley E, Te HS, Vargas HE, Brown R Jr, et al. An interferon-free antiviral regimen for HCV after liver transplantation. N Engl J Med 2014;371(25):2375-2382.
8. Limketkai BN, Mehta SH, Sutcliffe CG, Higgins YM, Torbenson MS, Brinkley SC, et al. Relationship of liver disease stage and antiviral therapy with liver-related events and death in adults coinfected with HIV/HCV. JAMA 2012;308(4):370-378.
9. van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA 2012;308(24):2584-2593.
10. Muhammad H, Hammami M, Ting P-S, Simsek C, Saberi B, Gurakar A. Can HCV viremic organs be used in liver Transplantation to HCV negative recipients? OBM Hepatol Gastroenterol 2020;4:1-8.
11. Ting PS, Hamilton JP, Gurakar A, Urrunaga NH, Ma M, Glorioso J, et al. Hepatitis C-positive donor liver transplantation for hepatitis C seronegative recipients. Transpl Infect Dis Dec 2019;21(6):e13194.
12. Cotter TG, Aronsohn A, Reddy KG, Charlton M. Liver Transplantation of HCV-viremic donors into HCV-negative recipients in the United States: increasing frequency with profound geographic variation. Transplantation 2021;105(6):1285-1290.
13. Gonzalez SA, Trotter JF. The rise of the opioid epidemic and hepatitis C-positive organs: A new era in liver transplantation. Hepatology 2018;67(4):1600-1608.
14. Kwong AJ, Wall A, Melcher M, et al. Liver transplantation for hepatitis C virus (HCV) non-viremic recipients with HCV viremic donors. Am J Transplant 2019;19(5):1380-1387.
15. Sobotka LA, Mumtaz K, Wellner MR, et al. Outcomes of hepatitis C virus seropositive donors to hepatitis C virus seronegative liver recipients: A large single center analysis. Ann Hepatol 2021;24:100318.
16. Ballarin R, Cucchetti A, Spaggiari M, Montalti R, Di Benedetto F, Nadalin S, et al. Long-term follow-up and outcome of liver transplantation from anti-hepatitis C virus-positive donors: a European multicentric case-control study. Transplantation 2011;91(11):1265-1272.
17. Selzner N, Berenguer M. Should organs from hepatitis C-positive donors be used in hepatitis C-negative recipients for liver transplantation? Liver Transpl 2018;24(6):831-840.
18. Edmonds C, Carver A, DeClercq J, Choi L, Peter M, Schlendorf K, Perri R, Forbes RC, Concepcion BP. Access to hepatitis C direct-acting antiviral therapy in hepatitis C-positive donor to hepatitis C-negative recipient solid-organ transplantation in a real-world setting. Am J Surg 2021 Sep 14:S0002-9610(21)00528-6. doi: 10.1016/j.amjsurg.2021.09.005. Epub ahead of print.