



ARTICLE OF THE MONTH

Linares I, Hamar M, Selzner N, Selzner M. Steatosis in Liver Transplantation: Current Limitations and Future Strategies. *Transplantation*. 2019;103(1):78-90.

Abstract:

In parallel with the pandemic of obesity and diabetes, the prevalence of nonalcoholic fatty liver disease has progressively increased. Nonalcoholic steatohepatitis (NASH), a subtype of nonalcoholic fatty liver disease has also augmented considerably being currently cirrhosis due to NASH the second indication for liver transplantation in the United States. Innovative treatments for NASH have shown promising results in phase 2 studies and are being presently evaluated in phase 3 trials. On the other hand, the high mortality on the liver transplant waitlist and the organ shortage has obligated the transplant centers to consider suboptimal grafts, such as steatotic livers for transplantation. Fatty livers are vulnerable to preservation injury resulting in a higher rate of primary nonfunction, early allograft dysfunction and posttransplant vascular and biliary complications. Macrosteatosis of more than 30% in fact is an independent risk factor for graft loss. Therefore, it needs to be considered into the risk assessment scores. Growing evidence supports that moderate and severe macrosteatotic grafts can be successfully used for liver transplantation with careful recipient selection. Protective strategies, such as machine-based perfusion have been developed in experimental setting to minimize preservation-related injury and are now on the verge to move into the clinical implementation. This review focuses on the current and potential future treatment of NASH and the clinical practice in fatty liver transplantation, highlights its limitations and optimal allocation, and summarizes the advances of experimental protective strategies, and their potential for clinical application to increase the acceptance and improve the outcomes after liver transplantation with high-grade steatotic livers.

COMMENTS MADE BY SCHLICHTING, NICOLETTE MD

Summary:

This review article, from the January 2019 issue of *Transplantation*, highlights how increasing rates of obesity and associated non-alcoholic fatty liver disease (NAFLD) are impacting the field of liver transplantation, both by increasing the number of patients in need of transplantation for

nonalcoholic steatosis (NASH) cirrhosis and by affecting the quality of available allografts due to higher rates of steatosis.

NASH cirrhosis is the second leading indication for liver transplantation, and while there are several ongoing clinical trials to evaluate medical treatments for NAFLD and NASH, none are currently recommended for clinical use. This review article summarizes the different medications under investigation with the goal of decreasing fat content, inflammation, and the resultant fibrotic changes.

The number of patients in need of a liver transplantation continues to exceed the number of available donors, leading to transplantation of liver allografts from extended criteria donors (ECD), which includes steatotic organs. Use of these marginal grafts is associated with increased rates of allograft dysfunction. Macrosteatosis is frequently discovered during organ procurement and is a common reason for graft discard. Transplantation of livers with mild steatosis (<30% macrosteatosis or any percentage of microsteatosis) is considered safe, however utilization of grafts with moderate (30-60% macrosteatosis) or severe (>60% macrosteatosis) steatosis is controversial and may be associated with higher rates of blood transfusion, post-reperfusion syndrome, allograft dysfunction, and longer hospital and ICU stays. Linares et al summarize the small studies that suggest that these grafts can be successfully transplanted, while suggesting that the results be interpreted with caution. The review article also describes the Balance of Risk (BAR) score that was developed and validated by Dutkowski et al using data from the United Network for Organ Sharing (UNOS) and the European Liver Transplant Registry. The BAR score stratifies organ recipients into three risk groups based on several characteristics, including age, MELD score, and cold ischemic time. Linares et al suggest that the successful transplantation outcomes with moderate macrosteatotic grafts noted in the previously described studies may be the result of carefully chosen recipients who fall into the low risk BAR group.

Utilization of machine perfusion techniques may prove useful in the future for the evaluation and optimization of marginal grafts prior to transplantation. This review article summarizes the currently available animal and clinical studies for each of the four described techniques, venous systemic oxygenated persufflation (VSOP), hypothermic oxygenated machine perfusion (HOPE), subnormothermic machine perfusion (SNMP), and normothermic machine perfusion (NMP). Further studies are needed before integration in to clinical practice occurs.

This review article provides an overview of the studies on medical treatments for NAFLD/NASH, outcomes following transplantation of steatotic allografts, and use of machine perfusion techniques. This is important for physicians who care for patients undergoing liver transplantation as NASH cirrhosis is currently the number two indication for liver transplantation and the inadequate supply of liver allografts has to led to increasing use of fatty allografts. Ideally, medical treatments will continue to advance as they did with hepatitis C thereby decreasing the number of patients with progression to NASH cirrhosis who will then require transplantation. Additionally, optimization of marginal grafts prior to transplantation could decrease the rates of reperfusion syndrome and allograft dysfunction, in addition to increasing the available organ supply for transplantation. As these areas of study continue to advance, they will have a significant impact on the transplant community.

References:

1. Linares I, Hamar M, Selzner N, Selzner M. Steatosis in Liver Transplantation: Current Limitations and Future Strategies. *Transplantation*. 2019;103(1):78-90.

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