My approach to the same consultation I received as a first-year fellow has drastically changed now that I am a third-year fellow. I now use a set of medical criteria to make informed recommendations regarding the patient's appropriateness for SLKT. Although the decision to allocate an organ or organs should never be made based solely on rules, we can now be more consistent with our decisions and optimize our organ use with the new allocation system. As a new member of the transplant nephrology community, I look forward to observing changes in the landscape of SLKT so we may continue to improve the allocation system and provide appropriate, guideline-based care for our kidney patients.

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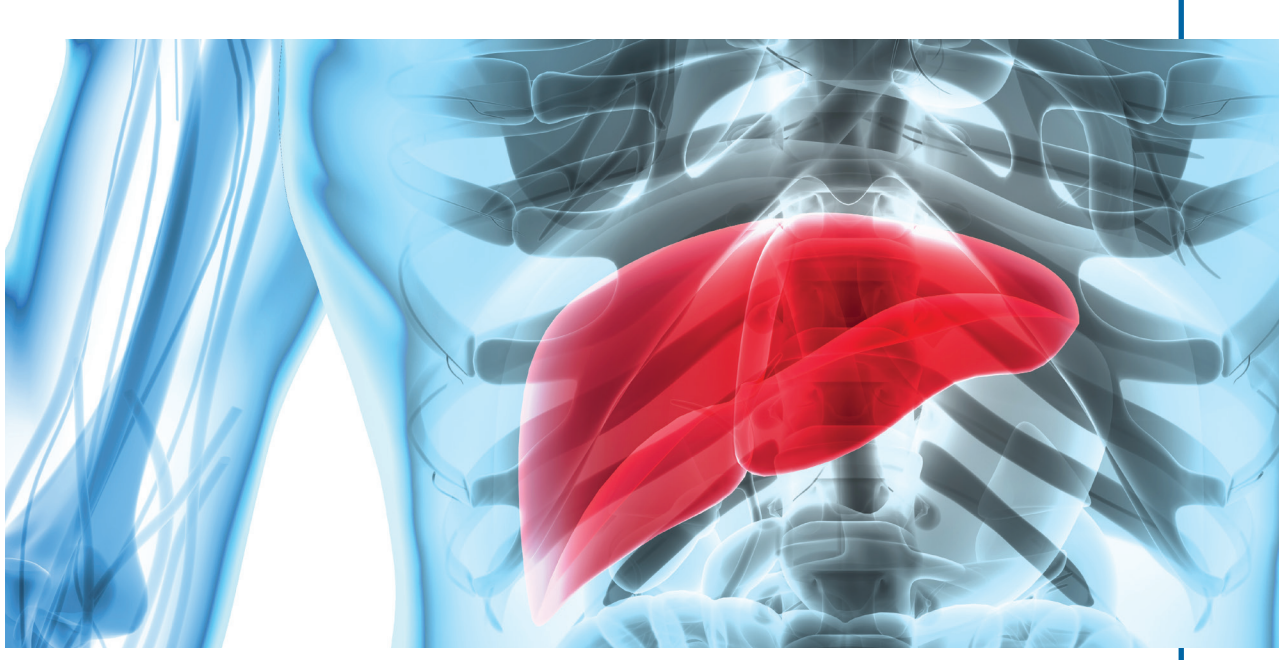
How Transplanted Livers Help Defend against Rejection in Multiple-Organ Transplantations

By Tracy Hampton



A new study points to factors involved in the reduced likelihood of rejection in liver-kidney transplant recipients compared with solitary kidney transplant recipients.

"For many years, transplant physicians and researchers have known that the liver transplant recipients require less immunosuppression than the recipients of other organs, to prevent rejection," said Timucin Taner, MD, PhD, a transplant surgeon at the Mayo Clinic and lead author of the *Kidney International* study. "This has been attributed to the liver being less immunogenic compared to the other commonly transplanted organs; however, the liver itself is an immunologically active organ, so we hypothesized that this phenomenon is more of an active process, brought about uniquely by the liver."

Over the past several years, Taner and his colleagues have systematically investigated this question by comparing the clinical outcomes of multiple organ transplant recipients, as well as the histologic and genetic changes that occur in the allografts of these patients. An earlier study revealed that, when compared with kidneys from solitary kidney transplant recipients, kidneys of simultaneous liver-kidney transplant recipients had fewer molecular markers of inflammation and T-cell activation and greater expression of genes associated with tissue integrity and metabolism

In this latest study of 28 simultaneous liver-kidney transplant recipients, 61 recipients of a solitary kidney, and 31 recipients of liver allografts, the phenotypic and functional characteristics of the circulating blood cells of the simultaneous liver-kidney transplant recipients resembled those of solitary liver transplant recipients and were associated with donor-specific hypo-alloresponsiveness.

Solitary kidney transplant recipients had more circulating CD8+ cytotoxic T cells, activated CD4+ and effector memory T cells, and interferon gamma–producing alloreactive T cells. Simultaneous liver-kidney transplant recipient T cells had a lower proliferative response to donor cells compared with solitary kidney recipients (11.9% vs. 42.9%), but their response to third party cells from a different donor was unaltered.

The results indicate that the circulating white blood cells of liver transplant recipients are less reactive to the transplanted organ than the same cells of kidney transplant recipients.

"In the current study, we demonstrate for the first time that the overall alloimmune responses in liver transplant recipients are downregulated while the immune responses to other antigens are preserved," Taner said.

He noted that the goal in any organ transplantation is to achieve long-term function of donor organs with minimal immunosuppression so as not to increase patients' risk for infection, cancer, and other issues.

"Given the findings of the current study and our previous publications, it appears that liver allografts have the unique ability to reduce the overall need for immunosuppression," Taner said. "Our goal is to find out the underlying mechanisms, so that novel therapeutic approaches could be used."

Such a strategy may help patients receiving various types of transplants reduce their need for anti-rejection drugs.

"These findings are significant as they provide the first evidence from a direct comparison of simultaneous liver-kidney and solitary graft recipients that the liver graft regulates host alloimmunity," noted Angus Thomson, PhD, DSc, Distinguished Professor of Surgery and Immunology at the University of Pittsburgh, who was not involved with this research. "While the study was not designed to elucidate underlying mechanisms, the findings suggest that identification of mechanisms may lead to design of improved therapeutic strategies in renal transplantation and other immune-mediated kidney disorders."