

Technique for preserving pre-transplant livers improves outcomes and organ pool

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Preserving organs on ice prior to transplantation, an approach known as cold storage or CS, has been the standard practice in liver transplant for 20 years. Now there is new evidence that a technique called hypothermic machine perfusion (HMP) may offer an improvement, according to the first-ever study comparing the impact of the two techniques on transplant outcomes.

The phase I study was carried out by Dr. James V. Guarrera and his colleagues at NewYork-Presbyterian Hospital/Columbia University Medical Center. The researchers found that HMP is at least as good as CS in preserving donor livers -- and that it most likely constitutes an advance over the traditional method. Improving preservation, they emphasize, could expand the availability of organs for transplantation.

Unlike cold storage, which Dr. Guarrera describes as a static technique, HMP dynamically simulates "aliveness" by providing a continuous flow of oxygen and key nutrients to the liver while diluting and removing toxins and waste products.

"Cold storage is the easy way to preserve vital organs for transplant. Generally, it has been a fairly effective way to keep a liver healthy en route to transplant surgery. But today, we have the technology to do better," says Dr. Guarrera, surgical director of adult liver transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center and assistant professor of surgery at Columbia University College of Physicians and Surgeons. "And by better preserving donor livers and



reducing preservation-related injury, we may be able to expand the pool of available organs, making liver transplantation available to more patients who need it."

The study compared 20 transplant patients who received HMP-preserved livers with 20 patients with CS-preserved livers, finding the first group experienced shorter hospital stays and fewer long-term complications. The HMP group also had lower levels of blood markers indicating injury to the liver that may have occurred during the preservation interval.

The findings are currently reported online in *The American Journal of Transplantation* and will be featured in the journal's February issue. The study was supported by a grant from the Health Resources and Services Administration, Division of Transplantation. A second grant is funding a phase II study.

Expanding Availability of Livers for Transplant

Improving organ preservation is especially important in light of major changes in the transplantation landscape, says Dr. Guarrera, and could broaden the availability of donor organs.

In the early days of liver transplantation, high-quality organs were plentiful for two reasons: First, liver transplantation had not yet become widespread, so demand was relatively low; and second, there was a greater supply of livers from young trauma victims. Thanks to a significant drop in violent crime and to public safety measures such as mandatory seat-belt use, the pool of young donors has shrunk -- and that's obviously a good thing, Dr. Guarrera notes. But there is no denying the stark fact that the age of the average liver donor is higher today, which means that the quality of available organs has deteriorated.

Dr. Guarrera goes on to describe the history and context of his interest in



HMP, a technique that dates back to the 1960s, when it was introduced for kidney preservation. It was soon dropped in favor of cold storage, deemed the simpler way to go. But then, in the 1990s, HMP made a comeback in kidney transplantation, coinciding with greater reliance on "imperfect" kidneys from older donors.

"We strongly suspected that HMP could be adapted to the <u>liver</u> transplantation setting," he says. "Our first challenge was to work with a manufacturer to make an HMP device more portable and more specific to the liver, an organ that is inherently more vulnerable to injury than the kidney. We've been using a pump produced by Medtronic, originally designed for use in cardiopulmonary bypass, combined with a preservation solution called Vasosol.

"Thus far, our results have been extremely encouraging. We just received FDA approval for a phase II study, focusing specifically on the effects of HMP in livers from 'extended criteria donors,' a group that makes up a growing proportion of the total number of donors today. Organs from these older, sicker donors are the ones most likely to benefit from machine perfusion."

Molecular and mechanistic studies also are under way. Establishing the benefits of HMP over CS will depend on the results of larger clinical studies, says Dr. Guarrera, but it is equally important to clarify the way the two techniques play out at a cellular and molecular level.

"We aim to show that even imperfect livers can be maintained in peak condition via HMP during the critical period when they are in transit from donor to recipient. It's the kind of 'quality improvement' that will translate into long-term benefits for patients."

Provided by New York- Presbyterian Hospital



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