

Blood-Pumping Device Preserves Hearts

BY MITCHEL L. ZOLER

Philadelphia Bureau

MADRID — A device that can preserve a donated heart for several hours with machine-pumped blood was used for the first time before a clinical heart transplant last January.

This successful use of warm, perfused heart maintenance before transplantation was the first of 20 planned heart transplants in the initial phase of a series of multicenter studies aimed at assessing the safety, efficacy, and feasibility of the organ care system (OCS), Dr. Bruce R. Rosengard said during a satellite symposium at the annual meeting of the International Society for Heart and Lung Transplantation.

The symposium was sponsored by TransMedics, a U.S. company that makes the OCS and is funding the clinical study. Dr. Rosengard is a coinvestigator on the trial but has no other financial relationship with TransMedics.

The OCS weighs about 70 pounds and is about the size of a compact refrigerator. The heart is removed from the donor, and a set of connecting tubes are placed in the aorta, pulmonary artery, and left atrium (if the donor's lungs are also removed for transplantation, the heart's left atrium is reconstructed using bovine pericardium), a procedure that's done during cold ischemia and generally takes less than 20 minutes. The heart is then placed in the perfusion module of the OCS, the tubes are hooked into the perfusion circuit, and 1,000-1,500 mL of the donor's blood is used to keep the heart perfused. The blood is fed with nutrients, such as amino acids and glucose, and kept at 34°-35° C.

In "dry-run" tests using human hearts

that could not be placed for transplant, the system has maintained the heart with no signs of ischemic damage for 6 hours, said Dr. Rosengard, professor and chairman of cardiac surgery at Cambridge University and Papworth Hospital, Cambridge, England.

The first time the OCS was used to preserve a heart prior to transplant into a patient was on Jan. 16 at the Clinic for Thoracic and Cardiovascular Surgery in Bad Oeynhausen, Germany. The heart was prepared while in cold ischemia for 16



A swine heart with connecting tubes (top right) sits in the OCS perfusion chamber.

minutes, and then warm blood perfusion was begun. Without use of the OCS, the estimated cold ischemia time would have been about 206 minutes, reported Dr. Gero Tenderich, a cardiothoracic surgeon and head of the heart transplant ward at the clinic. When the 55-year-old woman who received the heart was assessed at 7 and 21 days following transplantation, her

heart showed no signs of rejection or ischemic damage, Dr. Tenderich said.

The first 20 patients who receive hearts maintained this way will form the first phase of the Prospective Multi-Center European Trial to Evaluate the Safety and Performance of the Organ Care System for Heart Transplants (PROTECT) trial, which will enroll patients at Bad Oeynhausen and one other center in Germany, and at Papworth Hospital and one other center in England. If the maintenance strategy continues to be successful, the initial phase will be followed by study at additional European centers, said Dr. Rosengard.

Following that, the plan is to move into a realm with the best potential to significantly change heart transplantation. Using the OCS allows physicians to assess the functional capacity of a heart by echocardiography, ECG, and other measures before transplantation. This raises the prospect of transplanting hearts from marginal donors, including cardiac-death donors, if the organs prove to be functionally normal when tested while in the OCS. If this approach is successful, it could "dramatically increase the number of donor hearts," Dr. Rosengard said.

"My enthusiasm for this work could not be higher. I've been waiting for this day," commented Dr. Bartley P. Griffith, professor of surgery and chief of the division of cardiac surgery at the University of Maryland in Baltimore. "We weren't taught to question the standard approach to organ preservation, which is like fish on ice, but it's crazy. The future of transplantation requires reducing graft breakup and generation of danger signals." Dr. Griffith reported no financial relationship with TransMedics.

The organ care system is also being developed by TransMedics for preservation of lungs, livers, and kidneys. ■



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Single Antirejection Drug Is Better Than Two

BY MITCHEL L. ZOLER

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MADRID — Less immunosuppression was better than more for heart transplant patients, according to a report at the annual meeting of the International Society for Heart and Lung Transplantation.

Monotherapy with oral tacrolimus led to significantly better outcomes than did a combination of tacrolimus plus mycophenolate mofetil (MMF) in a randomized, controlled study of 58 heart transplant patients, said Dr. David A. Baran.

"Paradoxically, we showed a significant reduction in the total rejection burden with monotherapy," said Dr. Baran, research director of the heart failure treatment and heart transplant program at Newark (N.J.) Beth Israel Medical Center. The finding, from the first

prospective, controlled trial of tacrolimus monotherapy, "may herald the end of 'one size fits all' immunosuppression."

Dr. Baran acknowledged that the findings raise a fundamental question: Why should patients have less organ rejection with reduced immunosuppression? The answer is not yet clear, but he speculated that it may be linked to why transplant recipients generally have fewer rejection episodes the further out they progress from surgery. "It's possible that monotherapy allows more rapid 'aging' of the transplant," he said. The development of clinical tolerance might involve various immune mechanisms, such as clonal deletion or T-suppressor cells.

The study involved patients who received a first-time heart transplant at either Beth Israel or Mount Sinai Medical Center

in New York during April 2004 through August 2005. Following surgery, all patients were treated with oral tacrolimus and MMF, along with the steroid therapy that would continue for 2-5 months after surgery. Two weeks after surgery, the patients were randomized to either continue both tacrolimus and MMF or to tacrolimus alone. Drug discontinuation was nonblinded. During the next 6 months, eight of the patients randomized to receive combination therapy had to withdraw from their MMF regimen because of severe intolerance.

The study's primary end point was the average biopsy score at 6 months after transplantation. The average score was 0.60 in the combination-therapy group and 0.44 in the monotherapy group, a statistically significant difference that

showed less organ rejection in the monotherapy group.

Follow-up also showed fewer rejection episodes with monotherapy, especially during the first 90 days after surgery. Serum creatinine levels were similar in both groups.

One patient in the monotherapy group developed an asymptomatic episode of significant (class 3A) rejection, and was switched to combination therapy with MMF. Two patients in the combination therapy group also developed class 3A rejection, one of whom had hemodynamic compromise. Two other patients in the combination-treatment group became infected with cytomegalovirus.

The study was partially funded by Astellas Pharma Inc., which markets oral tacrolimus (Prograf). Dr. Baran does not have any financial relationship with Astellas. ■

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