

## Findings: American Transplant Congress

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### Communication Gaps Lead to Infections in Organ Recipients

By Daniel M. Keller

Delays and errors in communication from donor organ centers to recipient centers frequently contribute to the transmission of infections. Rachael Miller, MD, presented the results of a study of potential donor-derived infections reported between January 2008 and June 2010 to the Ad Hoc Disease Transmission Advisory Committee (DTAC) of the Organ Procurement and Transplantation Network, administered by the United Network for Organ Sharing (UNOS). Miller is clinical professor in infectious diseases at the University of Iowa Carver College of Medicine in Iowa City.

Communication gaps occur at multiple levels and have been associated with adverse outcomes in organ recipients, but effective communication can minimize or avert the transmission of infections. “If delays and errors in communication occur, they can have a significant impact on recipient morbidity and mortality,” Miller said.

Effective detection and management of potential donor-derived infections are made all the more difficult because of the complex and multiple channels of communication, including between donor and recipient transplant centers, diagnostic laboratories, and organ procurement organizations (OPOs) involved. “Clinicians may be unaware as to how to obtain and report relevant donor information,” Miller said.

The DTAC classifies donor-derived transmission events as proven, probable, or “intervention without documented transmission,” which typically means that an infection was averted through the use of antimicrobial therapy. For the study, a delay in communication was defined as lasting more than 3 days. An adverse event was an unexpected clinical infection, a more severe infection, or death.

The investigators identified 56 infection events involving 169 transplant recipients that met the study criteria for potential communication delays or errors. Thirty-eight events in 120 recipients were ultimately determined not to involve communication problems.

“However, 18 infection events were associated with communication delays or errors among 49 recipients,” Miller reported. Eleven of these cases involved bacterial infections, three viral, and four other or parasitic. Of these 18 occurrences, 12 (67 percent) were associated with an adverse event. Of the 20 recipients affected by an infectious adverse event, 6 died.

The researchers pinpointed several gaps involving many of the steps in the communication process. Some cases of communication error involved more than one step. In five instances, the transplant center delayed contacting the OPO to

relate a suspected donor-derived infection (range 22–56 days), and in three instances, the OPO delayed contacting the transplant center or the DTAC. There were also four failures of laboratories to relay donor results to the OPO and/or the transplant center, two communications of incomplete test results from the OPO to the transplant centers, and three clerical errors.

“The good news is that if prompt and effective communication was employed it allowed the opportunity for prompt intervention that either minimized or averted recipient infection,” Miller said. Of the 38 infection events without communication errors or delays, in 23 cases intervention positively influenced the outcome for 72 recipients. The remaining 15 events affecting 48 recipients required no intervention, or intervention had no effect on the outcome.

Communication can minimize or avert infections in transplant recipients, Miller said. In January the Organ Procurement and Transplantation Network implemented policy changes regarding communication, mainly concentrating on the procedures for OPOs and transplant centers to report and share donor-related information with relevant parties. Also, the involved parties should receive better education to help minimize communication problems and add to the safety of the donation process, Miller said.

Senior author of the study and DTAC chair Emily Blumberg, MD, professor of medicine and director of transplant infectious diseases at the University of Pennsylvania in Philadelphia, told *ASN Kidney News* that clinicians may not be aware that some infections are derived from donors and thus may not report them in a timely manner or at all.

Blumberg said one of her goals is to present her findings at meetings of transplant medical professionals and transplant administrators, and also at UNOS regional meetings, to raise awareness of the problem so people start to ask themselves, “Could this be [a] donor-derived [problem], and before letting this proceed further, can I notify people?” UNOS has implemented a contact process to encourage every transplant program to have a patient safety officer charged with promptly communicating a suspected problem to UNOS and to the OPO so that every center with an organ recipient will be notified.

Session chair David Foley, MD, associate professor of surgery at the University of Wisconsin in Madison, suggested that within each transplant center, “One safeguard measure would be a checklist for the surgeons to maybe potentially follow up with the OPO to make sure that no data have come back that have not been informed to us” concerning a donor. ●

### Shorter Steroid Course Lowers Cardiovascular Risks After Kidney Transplantation

By Daniel M. Keller

Early withdrawal of corticosteroids after kidney transplantation was associated with a lower rate of cardiovascular (CV) events compared with long-term corticosteroid administration, according to a study presented at the American Transplant Congress, held in Philadelphia from April 30 to May 4. Lead author Nicole Schmidt, PharmD, of the University of Cincinnati in Ohio, said that the decrease in CV events became apparent 3–4 years after transplant in the group of patients with early withdrawal, even though these patients had more coronary artery disease before transplant. There were no differences in overall patient survival or in CV-related deaths between the early corticosteroid withdrawal group and the long-term corticosteroid immunosuppression maintenance group, Schmidt said.

In general, CV disease accounts for about 30 percent of deaths among kidney transplant recipients. Schmidt said that clinical trials and a recent meta-analysis showed that corticosteroid avoidance or withdrawal has been associated with a decrease in CV risk factors, including new-onset diabetes, hypertension, hyperlipidemia, and weight gain. But, she said, “We still have limited long-term studies that have actually translated this cardiovascular risk reduction into actual [reduction in] cardiovascular events and ultimately, patient survival.”

The investigators therefore evaluated 1004 patients who received renal transplants between 1998 and 2010, 714 of whom underwent early withdrawal and 290 of whom were receiving long-term corticosteroid maintenance. Early withdrawal was defined as steroid withdrawal within 7 days after transplantation. This group tended to be older, had more men, had fewer African Americans, and had more coronary artery disease before transplant.

The early withdrawal group had fewer repeat transplants (9.5 percent) than did the long-term steroid group (14.5 percent), less delayed graft function (7.7 percent versus 15.2 percent, respectively), more HLA mismatches (mean 3.3 versus 2.1), but lower mean class II peak and current cytotoxic panel reactive antibodies.

In terms of immunosuppressive therapy, more of the early withdrawal patients were given tacrolimus (89.9 percent versus 51.7 percent) and sirolimus (22.1 percent versus 0.3 percent) and had less use of cyclosporin (9.1 percent versus 48.3 percent). More than 97 percent of each group was receiving mycophenolate mofetil. The long-term steroid maintenance group received mean steroid doses of 8.6 mg/day at 6 months and was still receiving a mean of 5.3 mg/day at 7 years.

The mean pre- and posttransplant total cholesterol was lower in the early withdrawal group compared with the long-term steroid group (168.6 versus 178.2 mg/dL and 172.9 versus 189.1 mg/dL, respectively. All other pre- and

posttransplant cholesterol values, including LDL cholesterol, did not differ significantly between the groups. Other CV risk factors were largely the same except that after transplant, patients in the long-term steroid group had a mean diastolic blood pressure that was 1.9 mm Hg higher, and they were taking more antihypertensive medications. The median follow-up times were 4.2 years for the early withdrawal group and 5.9 years for the patients receiving long-term steroid administration.

“Patients that received chronic steroid regimens experienced definitely more cardiovascular events than those that were withdrawn from steroids within 7 days after transplantation,” Schmidt reported. CV events occurred in 14 percent of the early withdrawal group and in 24.5 percent of the long-term steroid administration group. Kaplan-Meier analysis predicted 10-year CV event rates of 24 percent and 35 percent, respectively. The most common CV event experienced in both groups was angina.

The two groups did not show any significant difference in terms of patient survival. “When we looked at just the . . . cardiovascular-related deaths, we found, again, that there was no significant difference between the two groups,” Schmidt said.

Session co-chair Ram Peddi, MD, a transplant nephrologist at California Pacific Medical Center in San Francisco, raised the question whether longer follow-up might change the outcomes. Because there were some differences in demographic characteristics between the two groups at baseline, he suggested that a multivariate analysis should be performed to adjust for the differences.

In fact, Schmidt did present such an analysis in a later session during the conference. It showed that early steroid withdrawal was associated with a reduction of 54 percent in the risk of CV events (odds ratio [OR] = 0.459). Risk factors for the development of CV events were pretransplant diabetes mellitus (OR = 2.69) and smoking (OR = 1.88). The investigators concluded that when adjustment was made for multiple risk factors, their 12-year experience provides strong evidence for a protective effect of early corticosteroid withdrawal on CV events.

A third analysis from the same group of investigators showed that at 10 years, patient survival was 76 percent in both groups, and CV-related events accounted for 15 percent of the deaths for both.

Peddi said that it has long been known that patients can benefit in terms of CV disease if corticosteroids are withdrawn early. “I think we all are aware of the cardiovascular risks associated with corticosteroids, but [early withdrawal] is now possible with the newer immunosuppressive drugs that are available because especially the tacrolimus and mycophenolate and also the induction therapy offer better immunosuppression that is enabling us to take the patients off steroids,” he said. ●