Reduce Steroids to Tame Diabetes Post Transplant

Two studies show benefits with alemtuzumab induction therapy.

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

CHICAGO — Steroid minimization in patients undergoing heart transplantation may be associated with improved survival among patients with existing diabetes as well as a lower incidence of posttransplant, new-onset diabetes, according to research findings reported at the meeting.

In one retrospective study, survival was significantly lower in diabetic vs. nondiabetic transplant patients (about 65% vs. about 80%, respectively) when steroid immunosuppression was not minimized, but survival was similar (about 80% for diabetic vs. 85% for nondiabetic patients) in patients who did have steroid minimization, Dr. Jeffrey J. Teuteberg reported.

The first group included 200 patients who had transplants between 1998 and 2003 and received tacrolimus, mycophenolate, and gradual prednisone taper for immunosuppression. The second group consisted of 217 patients who underwent transplants between 2004 and 2008 and received tacrolimus, mycophenolate, and steroid minimization via rapid taper or alemtuzumab induction therapy, said Dr. Teuteberg of the Cardiovascular Institute at the University of Pittsburgh.

Steroid-free status at 3 years also was improved by steroid minimization. For example, almost all group 2 patients were steroid free at 3 years, compared with 75% of group 1 patients. Rejection rates were similar in both groups.

Differences between patient groups included older age, racial differences, less sensitization, and less ventricular assist device usage among the diabetic patients in group 2 vs. group 1.

"Clearly, there are multiple factors [influencing] why our patients with diabetes are doing better now" he said. A multivariate model is being developed to evaluate how strong a predictor diabetes is by era, and the investigators plan to examine more closely how comorbidities such as renal insufficiency and peripheral vascular disease affect outcomes.

Survival was significantly lower in diabetic vs. nondiabetic transplant patients when steroid immunosuppression was not minimized.

In another study from the University of Pittsburgh, the use of alemtuzumab induction followed by steroid-free maintenance immunosuppression in nondiabetic patients was associated with a lower incidence of new diabetes in the first 3 years after transplant, Raquel Jones reported.

That study included 110 heart transplant recipients who received alemtuzumab induction and 110 historical controls who received no induction therapy. The treatment and control groups had similar baseline characteristics, including body mass index, noted Ms. Jones, a medical student at the University of Pittsburgh.

Donor characteristics also were similar, except the treatment-group donors were significantly older (36 vs. 32 years) with longer ischemic times (209 vs. 171 minutes).

The treatment-group patients received alemtuzumab induction after October 2006, when the center began using such induction routinely. There were 110 control patients treated during October 2001–October 2006 without induction. Both groups received tacrolimus and mycophenolate for chronic immunosuppression, but the treatment group received dose-reduced tacrolimus and no steroids.

Steroid use in the control group at 6 months, 12 months, 2 years, and 3 years was 93%, 56%, 18%, and 0%, respectively, vs. 0% at all time points in the alemtuzumab induction group, Ms. Jones noted.

The baseline incidence of diabetes—defined as the use of any diabetic treatment—was 32% and 29% in the treatment and control groups, respectively. Fewer cases of new diabetes post transplant, relative to baseline, occurred in treatment group vs. the controls (8% vs. 44% of cases at 6 months; 8% vs. 29% of cases at 12 months; 7% vs. 22% of cases at 2 years; and 8% vs. 21% of cases at 3 years). New-onset cases in the noninduction group trended downward in tandem with steroid weaning.

No differences were seen between the two groups with regard to control and management of diabetes, including insulin use, at 3-year follow-up, Ms. Jones said.

Other data from this cohort reported at the meeting showed that alemtuzumab induction and steroid-free immunosuppression are associated with good survival and good rejection-free survival. Together, the findings contribute to the expanding evidence of the value of alemtuzumab induction with steroid-free maintenance in heart transplant patients. Previous studies have demonstrated its merit in other types of transplant, including renal and lung transplant.

Dr. Teuteberg and Ms. Jones discussed off-label use of alemtuzumab, but had no other relevant disclosures. ■

Gender Mismatch Means Lower 10-Year Transplant Survival

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

VITALS

Major Finding: Ten-year survival in gender-matched heart transplantation was 69%-71%, compared with 58%-59% in mismatched cases.

Data Source: A review of 857 heart transplant patients from between 1994 and 2008.

Disclosures: Dr. Kittleson reported that she had no relevant disclosures with regard to this presentation.

CHICAGO — Gender mismatch between heart donors and transplant recipients who were on triple-drug immunosuppression without induction therapy was associated with significantly lower 10-year survival, according to results of a study of 857 heart transplant cases.

The findings suggest that gender mismatch portends a poor prognosis in heart transplantation, Dr. Michelle Kittleson said at the meeting.

"The implications … are that maintaining sex matching in heart transplantation is beneficial, and these findings may impact donor selection and recipient wait time to transplant," she said.

'The implications … are that maintaining sex matching in heart transplantation is beneficial, and these findings may impact donor selection and recipient wait time to transplant.'

Previous studies showing decreased survival in gender mismatch heart transplant cases did not distinguish between immunosuppressive regimens or the use of induction therapy. So the current study was designed to evaluate the impact of gender mismatch in patients on standard triple-drug immunosuppression without induction therapy (tacrolimus, mycophenolate mofetil, and prednisone), explained Dr. Kittleson of the University of California, Los Angeles.

Dr. Kittleson and her colleagues assessed patients for 10-year actuarial survival and for freedom from allograft vasculopathy and nonfatal major adverse cardiac events, such as mycardial infarction, heart failure, percutaneous intervention, defibrillation, stroke, and new peripheral vascular disease.

Differences in survival between the gender-matched and gender-mismatched groups were statistically significant, but no significant differences were seen on the other outcome measures.

The investigators evaluated cases between 1994 and 2008 that included 506 with male-to-male (MM) donation, 132 with female-to-male (FM) donation, 113 with female-to-female (FF) donation, and 106 with male-to-female (MF) donation.

Ten-year survival rates in the four groups, respectively, were 69%, 58%, 71%, and 59%, Dr. Kittleson said.

Previous studies, such as one in which researchers used United Network for Organ Sharing data, have shown similar survival results with gender-mismatched transplantation with FM donation; most have suggested that female recipients are not affected by donor gender (Circ. Heart Failure 2009;2:401-8).

Although the mechanisms for this are unclear, several explanations have been suggested, such as immunologic effects and smaller heart size in FM donation, which provides inadequate functional reserve for males.

In the current study, however, both male and female recipient survival was affected by mismatched donor gender, which might be a factor of study design and follow-up, Dr. Kittleson noted.

For example, survival in FM donation decreased rapidly and remained lower throughout the 10-year period, compared with gender-matched donations, while survival in MF donation did not begin to diverge until after the 4th post-transplant year; some prior studies failed to extend follow-up long enough to identify this divergence.

Another study showing no survival differences in females enrolled patients over a longer time period, which could explain the difference. ■