

Kidney-Pancreas or Kidney-Islet Transplant Increased Function

Both types of transplant fared better than kidney-alone transplant in diabetic patients with end stage renal disease.

REVIEWED BY ANTONIO SECCHI, MD

In a group of type 1 diabetic patients, response to kidney-pancreas or kidney-islet transplant and the chance for kidney graft survival was better compared to kidney-only transplant.

Antonio Secchi, MD, and his colleagues showed that kidney-pancreas and kidney-islet transplants prevented graft vascular function from worsening. They also showed that renal resistance declined with either procedure. Dr. Secchi is from the San Raffaele Scientific Institute, Italy.

Patients enrolled were previously on a waiting list for kidney transplant and were treated for end stage renal disease (ESRD) by kidney-pancreas, kidney-islet or kidney-alone transplant. During this study, kidney-pancreas

transplant was performed simultaneously, and the procedure was performed in 166 patients. Islet transplant, performed in 24 patients, was done ≥ 1 year after kidney transplant in all but six of the patients in this group.

COMBINATION TRANSPLANTS

Investigators examined and tracked the kidney graft size, survival, hypertrophy and vascular function of the transplanted kidney in 234 patients. They found that kidney transplants produced better results when they were performed in combination with pancreas or islet transplant. "Pancreas and islet transplantations confer adjunctive benefits for kidney graft survival in ESRD type 1 diabetic patients," the investigators wrote in

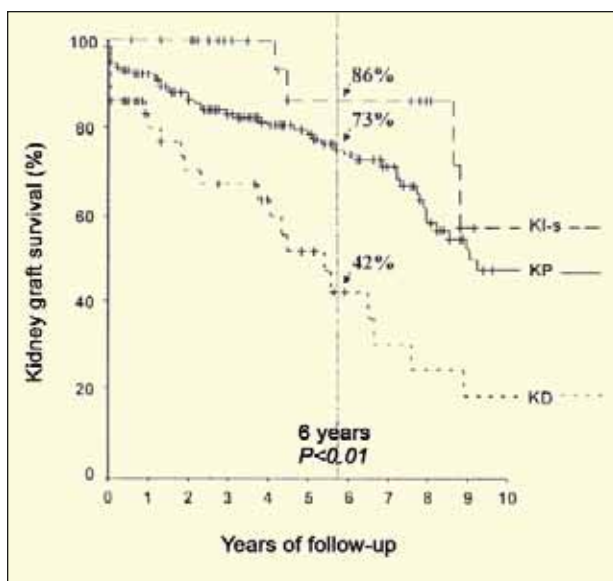


Figure 1. Kidney graft survival after 10 years.

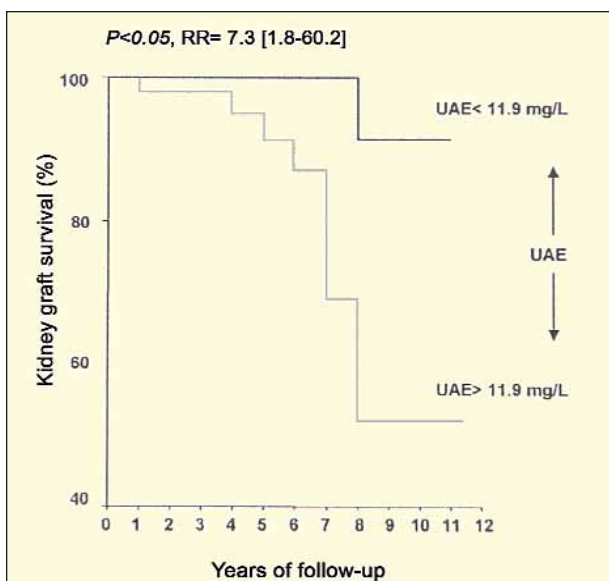


Figure 2. Kidney graft survival after 12 years.

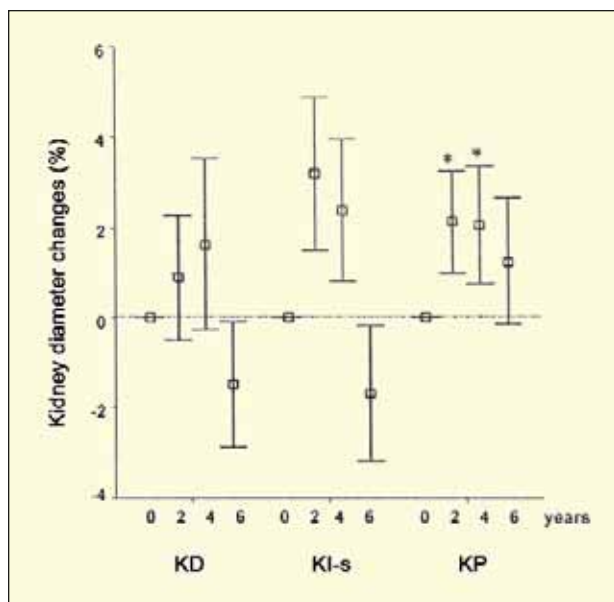


Figure 3. Kidney diameter change after 6 years.

Diabetes Care.

When nitric oxide (NO) pathways are altered in diabetic patients, diabetic nephropathy may result. If transplantation of the pancreas or islet occurs, and if insulin independence results, there is a possibility to prevent diabetic nephropathy. In addition, transplanting these organs may improve graft survival as well as recover kidney function, the investigators wrote.

"Expression of [nitric oxide synthase] NOS in the kidney graft correlated well with the functional data, showing an early impairment of NO pathways in the glomerular vessels of [kidney-alone]-transplanted patients," they wrote. When kidney-pancreas or kidney-islet transplants were performed, the NOS expression was less inhibited.

MEASURE OF KIDNEY FUNCTION

At baseline, which investigators defined as hospital discharge after transplant, and then yearly for 6 years, Dr. Secchi and colleagues measured kidney function (Figures 1,2). The evaluation of kidney size (Figure 3), renal arterial resistance index, microalbuminuria and kidney NOS determined the level of function. Investigators also evaluated urinary albumin excretion (UAE) and performed kidney biopsies.

An abnormality in UAE and resistance index (RI) levels occurs during preclinical diabetic nephropathy, and it is an indication for renal dysfunction. According to the investigators, if UAE increased, there was a strong indication that the kidney transplant would fail in type

1 diabetic patients with ESRD. Patients in the kidney-alone transplant group had a higher rate of kidney rejection compared to the kidney-islet transplant and kidney-pancreas groups (0.7 ± 0.1 vs 0.2 ± 0.1 and 0.4 ± 0.1 , respectively, $P < .05$).

GRAFT SURVIVAL

Investigators noted that the presence of high UAE levels also predicted poor graft survival in both the kidney-pancreas and kidney-alone transplant groups. At 2, 4 and 6 years, graft survival – which was determined by the need for dialysis treatment – and vascular function were better in the kidney-pancreas and kidney-islet groups compared to the kidney-alone group. Investigators noted that at 6 years, the rates of survival were: 86% in kidney-islet transplant patients, 73% in kidney-pancreas patients and 42% in kidney-alone patients ($P < .01$).

Between baseline and year 6, patients in the kidney-alone group had a significantly lower mean UAE (31.4 ± 9.0 vs 82.9 ± 33.6 mg/dL, $P < .05$). The reverse was true of the kidney-pancreas and kidney-islet groups. When these two groups were compared, patients who underwent kidney-pancreas transplant had the lowest UAE levels at both 2 and 4 years ($P < .01$), the investigators wrote.

KIDNEY-PANCREAS TRANSPLANT

Renal arterial RI improved over the study, but only in the kidney-pancreas and kidney-islet groups (0.74 ± 0.1 to $0.68 \pm 0.01\%$, $P < .01$ and 0.72 ± 0.02 to $0.69 \pm 0.02\%$, $P < .05$, respectively). At 4 years, resistance was the lowest in the kidney-pancreas group. This was statistically significant.

Concluding their study, Dr. Secchi wrote that type 1 diabetic patients with ESRD are susceptible to the effects of diabetic nephropathy – including the worsening of vascular kidney function and possible graft failure – even after kidney transplant. "It is possible that restoration of full endocrine function in the pancreas, or at least partial beta-cell function, could lead to improved NOS expression in the kidney and thereby ameliorate kidney vascular function," he wrote. Therefore, kidney-pancreas or kidney-islet transplants should be considered before kidney-alone transplant. ■

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Fiorina P, Venturini M, Folli F, et al. Natural History of Kidney Graft Survival, Hypertrophy, and Vascular Function in End-Stage Renal Disease Type 1 Diabetic Kidney-Transplanted Patients. *Diabetes Care*. 2005;28:1303-1310.