Kidney transplants can be life-savers for many patients with chronic kidney disease. Still, a significant number of transplanted kidneys are rejected or do not function properly over time. Physicians have been reluctant to remove these organs, but a recent study indicates that such a transplant nephrectomy can offer significant survival benefits for patients (Ayus JC, et al. J Am Soc Nephrol 2010; 21:374–380). While additional studies are needed, the results indicate that clinicians should rethink how they treat patients with failed kidney allografts.

“Our results raise questions about the current clinical paradigm and suggest that routine allograft nephrectomy in stable dialysis patients with a failed renal allograft should be evaluated against current management strategies in a randomized trial as a possible strategy for improving outcomes among this growing population of high-risk patients with end stage renal disease,” the authors wrote.

Options after allograft failure

Patients with chronic kidney disease often must wait years for a suitable kidney transplant (and some die while on the waiting list), but their return to health is not ensured once they receive a donor kidney. A growing number of patients are returning instead to dialysis after a failed kidney transplant, where they face an increased risk of complications and premature death.

The problem will likely become more widespread, as the prevalence and incidence of end stage renal disease are projected to increase substantially in the United States over the next several decades.

Nephrectomy following failed kidney transplant can yield significant benefits for some patients.

Researchers Discover Gene for Devastating Kidney Disease

A recent genetic discovery may provide clues to the mysteries behind focal segmental glomerulosclerosis (FSGS), the second leading cause of kidney failure in children and the most prevalent acquired kidney disease leading to transplantation among pediatric patients (Brown E, et al. Nature Genet 2010; 42:72–76).

Investigators have found that mutations in the INF2 gene occur in a large numbers of families with affected members and may be relevant for understanding how the disease originates.

“We are hopeful these new findings will impact future clinical studies and patient care,” said Henry Brehm, executive director of the nonprofit NephCure Foundation, which helped fund the study. These latest research findings could not come soon enough, as prevention and treatment options for patients with FSGS are sorely needed. Patients today are treated with steroids, must undergo dialysis, and often require a kidney transplant. In 20 percent to 50 percent of transplant cases, the disease recurs in the transplanted kidney, sometimes within hours. Over half of the patients with recurrent FSGS in their transplant will lose their kidney within five years.
Physicians have wrestled with whether to remove failed kidney allografts in these patients, not knowing how such an extensive surgery would affect the health and survival of individuals receiving chronic dialysis. Many have assumed that the operation would be too risky and would increase patients' immunoreactivity—presumably due to increased exposure to foreign antigens during the nephrectomy operation. The thought is that this increased immunoreactivity would decrease these patients' chances of receiving a future transplant.

Outcomes following nephrectomy

To investigate the costs and benefits of transplant nephrectomy in patients with failed kidney allografts, Juan Carlos Ayus, MD, FASN, director of clinical research at Renal Consultants of Houston, and his colleagues studied information from all adults who underwent a single kidney transplant or two nonsequential kidney transplants and returned to chronic dialysis after kidney allograft failure between January 1994 and December 2004. Data were obtained from the U.S. Renal Data System (USRDS). The researchers excluded patients in whom the kidney allograft did not survive at least three months, as well as those who died within less than one day after kidney allograft failure, those who died within less than one day after kidney allograft failure, those who died within less than one day after kidney allograft failure, and those who died within less than one day after kidney allograft failure. The primary outcome was death from any cause through December 31, 2004, which was identified from USRDS files. The mean follow-up was 2.93 ± 2.26 years.

Among 10,951 transplant recipients who returned to chronic dialysis, 3451 (31.5 percent) received an allograft nephrectomy during follow-up. These patients returned to dialysis at a median time of 1.66 years (interquartile range: 0.73 to 3.02 years). The investigators found that receiving an allograft nephrectomy was associated with a 32 percent lower risk for death from all causes after adjusting for sociodemographic characteristics, comorbidity burden, donor characteristics, interim clinical conditions associated with receiving allograft nephrectomy, and propensity to receive an allograft nephrectomy. Even after Ayus and his team performed six additional sensitivity analyses including or excluding specific patient subgroups, there were no clinically relevant differences in the estimated benefits associated with the nephrectomy.

For patients who underwent a transplant nephrectomy, the rate of death within 30 days of the surgery was only 1.5 percent (53 deaths).

The investigators also found that patients who received a transplant nephrectomy were more than twice as likely to receive a second transplant during the follow-up period than those who did not undergo a nephrectomy of the initial failed allograft (10 percent versus 4.1 percent, p < 0.001). It is unclear why patients who received a transplant nephrectomy had an increased rate of repeat transplantation. The researchers suspect the increased transplantation rate may reflect better health in the nephrectomy group through either lower comorbidity or improved health status following nephrectomy due to reduced chronic inflammation.

The investigators made several postulations after analyzing their findings. They suspect that patients with failed transplants experience higher death rates due to chronic inflammation. In addition, patients who retain a failed renal allograft routinely use low-dose immunosuppressive therapies after returning to dialysis, which may delay the need for ultimate nephrectomy and contribute to an increased risk of cardiovascular and infectious complications.

Nephrectomy “spares the patients unnecessary immunosuppressive therapy and more importantly removes a source of chronic inflammation that predisposes to morbidity and mortality on dialysis,” said William Bennett, MD, who was not involved with the research. Bennett is medical director of kidney transplantation at Legacy Good Samaritan Hospital in Portland, Oregon.

According to Ayus, this is the first study to use a very sophisticated and large
Failed Transplant

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database to suggest a significant survival advantage with transplant nephrectomy and a very low mortality with this type of operation. “More importantly, the study has dispelled the notion that transplant nephrectomy reduces the chance for re-transplantation when in fact our study shows for the first time that in the group of patients who underwent transplant nephrectomy, the rate of re-transplantation was significantly higher compared with the non-nephrectomy group,” he said. This finding argues against withholding a transplant nephrectomy due to a presumed reduced chance of repeat transplantation, the authors wrote. The research results challenge the traditional practice of retaining kidney allografts after transplant failure. “This is indeed an important article addressing a difficult management point in transplantation management,” Bennett said. “The paper gives us clear guidance on the preferability of allograft nephrectomy for failed grafts.” While this study is the largest and most rigorous thus far, it is not a randomized clinical trial, which is the gold standard in epidemiology, Ayus said. “Our study only indicates a very strong association between transplant nephrectomy and increased survival,” he said. “Until the randomized study is done (if ever), this information is the strongest evidence that physicians could use to improve survival in patients who return to dialysis with a failed allograft.” Ayus said he hopes that additional rigorous studies are performed to provide more definitive information on the value of transplant nephrectomy following failed kidney allografts.

ASN News

New Archives Effort Will Document ASN and Nephrology History

In honor of ASN’s 50th anniversary in 2016, the society is developing an archives program to document important milestones in the history of ASN and nephrology. ASN seeks volunteers to assist the society in identifying pivotal moments in ASN history and the most important advances in kidney treatment and research. Please let us know if you are interested in participating and contributing to our archiving efforts. One way you may wish to contribute is by sharing materials you have from ASN meetings, publications, or other activities. If you have material you think may be of interest, please contact Shari Leventhal at archives@asn-online.org or call her at 202-416-0658 to discuss your potential contributions.

ASN will underwrite the costs of copying and shipping material that we do not already possess and that needs to be added to the archives. We have included some images of ASN attendees during past Renal Week meetings and encourage you to guess who they are. You will find the key on page 23 to help you find out if you were right.

ASN invites our members to contribute to this exciting endeavor. As we look toward the future with the arrival of 2010, let us celebrate the past by building our archives program!

Guess the Nephrologist

A.

B.

C.

D.