Allograft Nephrectomy after Transplant Failure: Should It Be Performed in All Patients Returning to Dialysis?

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doi: 10.1681/ASN.2009121262

Although considerable advances in the field of transplantation have improved short-term outcomes, little impact has been made on the long-term success of transplant allografts. As a result, a substantial proportion of patients will ultimately return to dialysis and the milieu of ESRD. Approximately 20% of all renal patients on the transplant waiting list in the United States have had a previously failed allograft. This population has high mortality with 10-yr survival of <40% and with some suggesting that continued efforts to maintain the allograft through the use of low-dosage immunosuppression as contributing. In this issue of JASN, Ayus et al. report that patients who have failed allografts, return to dialysis, and undergo allograft nephrectomy have improved survival as compared with those in whom the allograft is retained. This is an interesting finding and one that will generate considerable discussion in the transplant community and further fuel the debate regarding the role of transplant nephrectomy in the treatment of this particular subset of patients.

We agree there may be beneficial effects of transplant nephrectomy, but one should not generalize the findings of Ayus et al. recommending removal of allografts to all patients without considering the limitations of their study. First and foremost, this is a retrospective interrogation of the US Renal Data System database with their results being subject to the methodologic limitations of database reviews. The population evaluated is limited to patients who had Medicare as the primary payer, and files for Medicare claims with CPT codes for allograft nephrectomy are used to determine who had their transplant removed. This may limit to some degree the applicability of their findings to other patient populations.

In examining the results of Ayus et al., patients who underwent allograft nephrectomy were significantly younger, had fewer comorbid conditions, and were more likely to receive treatment for rejection with antibody preparations and steroids. Comorbid conditions were determined from the US Renal Data System 2728 Medical Evidence Form completed closest to the start of dialysis. One could obviously argue that the reason for the decreased mortality in the group of patients undergoing nephrectomy was that they were a younger, healthier population as compared with those with retained transplants, who may have been considered too high risk to undergo a surgical procedure. To address this treatment selection bias, the authors performed regression analyses to adjust for characteristics that differed between the two groups and found that survival, when adjusted for all factors, associated independently with allograft nephrectomy. We agree with the authors as stated in their discussion, despite these statistical methods, their analysis remains susceptible to the effects of residual confounding and selection bias.

The authors hypothesize that excess mortality in the group with retained transplants may be due to an ongoing inflammatory state. In fact, in a previously published study, the authors showed prospectively that patients who had failed allografts and clinical symptoms and underwent nephrectomy had enhanced responsiveness to erythropoietin, resolution of hypoalbuminemia, and improvement in the biochemical markers of chronic inflammation. Our group has shown similar findings. In a retrospective review of 345 patients with failed kidney transplants, 79% of patients ultimately required nephrectomy primarily for clinical symptoms. Upon histologic examination of the resected transplant specimens, significant inflammation was noted in the vast majority. One must realize that in both populations, patients who underwent nephrectomy had associated clinical symptoms, and, as such, the results may not be generalizable to asymptomatic patients with failed allografts.

Ayus et al. also suggest that ongoing use of low-dosage immunosuppression contributes to excess mortality by increasing the risk for cardiovascular and infectious complications. Although hypothesis generating, no definitive conclusions can be made because the routine use of immunosuppression after transplant failure is not available in the United Network for Organ Sharing database. It would be interesting to examine the characteristics of patients who have ESRD and remain on long-term low-dosage immunosuppression as compared with those who are weaned completely off to determine whether those who are weaned off and remain asymptomatic have fewer comorbid complications and lower biomarkers of inflammation.

Ayus et al. make a solid case for allograft nephrectomy after return to dialysis, but it is necessary to consider the reasons that this might not be appropriate for all patients. The obvious argument is that a surgical procedure with associated hazards may be too high risk for some patients. A study of 70 consecutive patients who underwent allograft nephrectomy showed that almost 50% required transfusion in the perioperative period and that 15% had major...
surgical complications, with infection being the most frequent.\textsuperscript{6}

Another argument is that removal of the graft leads to immunoreactivity and increased panel-reactive antibodies. In a similar retrospective review of the United Network for Organ Sharing database, Johnston \textit{et al.}\textsuperscript{7} noted significantly higher panel-reactive antibodies before repeat transplantation in patients who had undergone allograft nephrectomy. In patients with first graft survival \( \geq 12 \) months, allograft nephrectomy was associated with an increased risk for repeat transplant failure, suggesting there may be some benefit for retransplantation by leaving the failed graft in place. Ayus \textit{et al.}\textsuperscript{3} note increased rates of repeat transplantation in patients who underwent allograft nephrectomy but do not comment on overall survival of those grafts.\textsuperscript{5}

We agree that the finding noted by Ayus \textit{et al.}\textsuperscript{3} that allograft nephrectomy associates with improved survival is important and hypothesis generating. With a growing number of patients returning to dialysis after a failed transplant, it is vital to optimize their treatment and to consider the potential role of nephrectomy in this subset with high morbidity and mortality. Further studies should be carried out in an appropriately designed prospective manner.

**DISCLOSURES**
None.

**REFERENCES**
