

Procurement Biopsies in Kidneys Retrieved for Transplantation

Sayeed Khan Malek

Clin J Am Soc Nephrol 9: 443–444, 2014. doi: 10.2215/CJN.00470114

A shortage of deceased donor organs continues to be a persistent problem in kidney transplantation. The number of candidates on the waiting list continues to increase each year while organ donation rates remain flat. Importantly, many kidneys recovered for transplantation are discarded, and discard rates are increasing. The discard rate increased steadily from 12.7% in 2002 to 17.9% in 2011 (1,2). Of the kidneys recovered for transplantation and not used, the biopsy finding is the major reason given for discard. Living donation rates have also remained unchanged over the past decade despite the introduction of paired kidney exchanges, as well as novel desensitization protocols. Given the continued organ scarcity, both for living and deceased donors, it is vital that we maximize every opportunity for organ utilization and improve our understanding of why recovered kidneys are not being transplanted.

In this edition of *CJASN*, using data from the United Network for Organ Sharing and the Scientific Registry of Transplant Recipients, Kasiske *et al.* (1) perform a retrospective, observational, case-controlled study by examining results from biopsies performed in 2010 of 83 kidneys discarded due to findings and compare them with 83 contralateral transplanted kidneys from the same donor, as well as 83 randomly matched deceased donors with the same donor risk profile. They found significant overlap in biopsy findings between transplanted and discarded kidneys and noted that glomerulosclerosis >20% was independently predictive of discard. One-year graft survival of contralateral transplanted kidneys was lower compared with that of all deceased donor kidney recipients (79.5% versus 91.6%), but was still acceptable in their estimation. Long-term outcomes were not discussed and prior studies would suggest that they are inferior and less acceptable. Kasiske *et al.* conclude that routine use of biopsies could lead to unnecessary kidney discards, and that this practice should be abandoned or critically re-examined in controlled trials.

The use of procurement biopsies has become an increasingly common practice, particularly in expanded criteria donor kidneys. A donor kidney biopsy can demonstrate chronic changes, as well as the degree of pathologic deterioration, and help with the assessment of the kidney's suitability for transplantation. Interpretation of a donor kidney biopsy, however, requires a meticulous evaluation of the degree of

glomerulosclerosis, vessel arteriosclerosis, vessel hyalinosis, and interstitial fibrosis. Previous studies (3–9) have demonstrated considerable variability in biopsy findings based on the type of biopsy (wedge versus needle), sample size, experience of the pathologist, and inconsistency in reporting biopsy findings. Almost all the biopsies were evaluated by frozen section because they need to be read as soon as possible. Frozen section evaluation provides information about interstitial fibrosis, vessel arteriosclerosis, and glomerulosclerosis, but does limit interpretation. Rapid processing protocols can facilitate permanent section evaluation and provide more detailed information within 2–4 hours, but they require that both a pathologist and a technician be on call 24 hours a day, 7 days a week.

Controlling for these variables has proven to be a difficult endeavor. It has been suggested that kidneys with glomerulosclerosis >20% should not be used for transplantation. Other studies have shown that kidneys with glomerulosclerosis >20% had similar prognoses compared with those with less extensive glomerular changes. Wedge biopsies can overestimate the total amount of glomerulosclerosis because of the predominance of sclerosis in the subcapsular region of the kidney. This can result in refusal of kidneys that may otherwise be suitable for transplantation. Needle biopsies allow sampling of deeper tissue, but with a lower amount of total tissue per sample. Donor vascular disease is another important parameter that is often not reported consistently in biopsy findings and is noted to be an independent risk factor for suboptimal graft survival.

There are several limitations to the use of registry data in the analysis of procurement biopsies in kidney transplantation. Apart from the variability in sampling and interpretation noted above, there is always a potential for selection bias. Biopsies are more likely to be obtained when the donor kidney is suspected to be suboptimal. Moreover, one can only study risk factors in kidneys that were selected for transplantation. In this regard, Kasiske and colleagues, by looking at donors where one kidney was transplanted and the other mate kidney discarded and comparing them with a cohort of matched deceased donor kidneys with a comparable risk profile, have demonstrated that information from procurement biopsies is of low quality and leads to unnecessary discard of transplantable kidneys. Biopsies

Transplant Surgery, Brigham & Women's Hospital, Boston, Massachusetts

Correspondence:

Sayeed K. Malek, Brigham and Women's Hospital, Transplant Surgery, 75 Francis Street, Boston, MA 02115. Email: smalek@partners.org

are rarely performed in the Eurotransplant experience where discard rates are low. However, Remuzzi *et al.*, in a European study, has shown that the risk of graft failure in recipients >60 years was 3.6 times more likely when transplanted kidneys were not biopsied (4). Should we then study biopsy practices in a more controlled environment or should we give them up altogether?

In a related multi-center study also published in this edition, Hall *et al.* (10) look at acute tubular necrosis (ATN) in preimplant biopsies and allograft outcomes. They reviewed 651 kidneys biopsies over a 2 year period (March 2010 to April 2012) and reported a 17% incidence of ATN. The primary outcome of the analysis was delayed graft function (DGF) and the secondary outcome was death-censored graft failure. Their study demonstrated a 40% rate of DGF and 6% experienced graft failure. Looking at kidneys with and without ATN in preimplant biopsies, DGF occurred in 45% of kidneys with ATN and in 39% of kidneys without ATN. Graft failure was not significantly different in the two groups (8% versus 5%). However, in stratified analysis, the adjusted relative risk for DGF with ATN was higher for donation after cardiac death (DCD) kidneys than for non-DCD kidneys. In their opinion, there was little evidence to suggest that a preimplant biopsy finding of ATN is useful when making the decision regarding acceptance or rejection of donor kidneys. However, the confidence intervals were wide and, therefore, with-ATN group may be at higher risk of DGF and graft failure. DCD kidneys are associated with a 20% increased incidence of DGF. Other factors, such as cold ischemia time, also contribute to DGF. It has been demonstrated that when cold ischemia time is limited to <12 hours, the rate of DGF in DCD kidneys (25.2%) approaches that of standard criteria donor SCD kidneys. Both of these studies highlight the limitations of using biopsy results as the sole criterion for turning down donor kidneys.

Another important issue affecting transplant centers is the intense scrutiny and regulatory oversight of post-transplant outcomes (11). Centers that fail to meet performance metrics are subject to quality review, a Systems Improvement Agreement, and the potential loss of funding. The primary outcomes used to evaluate a center are 1-year graft and patient survival. One of the unintended consequences of this regulatory oversight is the adoption of a risk-averse strategy by transplant centers whereby low performing centers may refuse donor kidneys presumed to be of high risk, such as those with poor biopsy findings.

The decision to transplant a particular kidney is complex and dependent on a multitude of factors, including donor age, clinical history, anatomic abnormalities, terminal creatinine, and biopsy findings. When the biopsy findings are consistent with the clinical evaluation of the donor, they are useful in making the determination about transplanting the kidney. However, biopsy findings considered in isolation are of limited value and should be interpreted with caution when making the decision to turn down a potentially

transplantable kidney. Given the ongoing shortage of donors, more clinical trials and randomized multi-center studies need to be conducted to better elucidate the role of procurement biopsies in decision making regarding acceptance of donor kidneys for transplantation.

Disclosures

None.

References

1. Kasiske BL, Stewart DE, Bista BR, Salkowski N, Snyder JJ, Israni AK, Cray GS, Rosendale JD, Matas AJ, Delmonico FL: The role of procurement biopsies in acceptance decisions for kidneys retrieved for transplant. *Clin J Am Soc Nephrol* 9: 562–571, 2014
2. Scientific Registry of transplant Recipients: 2011 Annual report. Available from: <https://www.ustransplant.org>. Accessed January 6, 2014
3. Pokorná E, Vítko S, Chadimová M, Schück O, Ekberg H: Proportion of glomerulosclerosis in procurement wedge renal biopsy cannot alone discriminate for acceptance of marginal donors. *Transplantation* 69: 36–43, 2000
4. Remuzzi G, Cravedi P, Perna A, Dimitrov BD, Turturro M, Locatelli G, Rigotti P, Baldan N, Beatini M, Valente U, Scalomogna M, Ruggenti P; Dual Kidney Transplant Group: Long-term outcome of renal transplantation from older donors. *N Engl J Med* 354: 343–352, 2006
5. Randhawa PS, Minervini MI, Lombardero M, Duquesnoy R, Fung J, Shapiro R, Jordan M, Vivas C, Scantlebury V, Demetris A: Biopsy of marginal donor kidneys: correlation of histologic findings with graft dysfunction. *Transplantation* 69: 1352–1357, 2000
6. Gaber LW, Moore LW, Alloway RR, Amiri MH, Vera SR, Gaber AO: Glomerulosclerosis as a determinant of posttransplant function of older donor renal allografts. *Transplantation* 60: 334–339, 1995
7. Kayler LK, Mohanka R, Basu A, Shapiro R, Randhawa PS: Correlation of histologic findings on preimplant biopsy with kidney graft survival. *Transpl Int* 21: 892–898, 2008
8. Muruve NA, Steinbecker KM, Luger AM: Are wedge biopsies of cadaveric kidneys obtained at procurement reliable? *Transplantation* 69: 2384–2388, 2000
9. Sung RS, Christensen LL, Leichtman AB, Greenstein SM, Distant DA, Wynn JJ, Stegall MD, Delmonico FL, Port FK: Determinants of discard of expanded criteria donor kidneys: impact of biopsy and machine perfusion. *Am J Transplant* 8: 783–792, 2008
10. Hall IE, Reese PP, Weng FL, Schröppel B, Doshi MD, Hasz RD, Reitsma W, Goldstein MJ, Hong K, Parikh CR: Preimplant histologic tubular necrosis and allograft outcomes. *Clin J Am Soc Nephrol* 9: 573–582, 2014
11. Schold JD, Buccini LD, Srinivas TR, Srinivas RT, Poggio ED, Flechner SM, Soria C, Segev DL, Fung J, Goldfarb DA: The association of center performance evaluations and kidney transplant volume in the United States. *Am J Transplant* 13: 67–75, 2013

Published online ahead of print. Publication date available at www.cjasn.org.

See related articles, “The Role of Procurement Biopsies in Acceptance Decisions for Kidneys Retrieved for Transplant,” and “Preimplant Histologic Acute Tubular Necrosis and Allograft Outcomes,” on pages 562–571 and pages 573–582 respectively.