The Role of Procurement Biopsies in Acceptance Decisions for Kidneys Retrieved for Transplant

Bertram L. Kasiske,† Darren E. Stewart,‡ Bipin R. Bista,§ Nicholas Salkowski,* Jon J. Snyder,*‖ Ajay K. Israni,*†‖ Gretchen S. Crary,¶ John D. Rosendale,‡ Arthur J. Matas,** and Francis L. Delmonico††*

*Scientific Registry of Transplant Recipients, Minneapolis Medical Research Foundation, Minneapolis, Minnesota; †Department of Medicine and ¶Department of Laboratory Medicine and Pathology, Hennepin County Medical Center, Minneapolis, Minnesota; ‡Organ Procurement and Transplantation Network, United Network for Organ Sharing, Richmond, Virginia; §Departments of Medicine and **Surgery, and ‖Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, Minnesota; and ††New England Organ Bank, Waltham, Massachusetts

Correspondence: Dr. Bertram L. Kasiske, Division of Nephrology, Department of Medicine, Hennepin County Medical Center, 701 Park Avenue, Minneapolis, MN 55415. Email: kasis001@umn.edu

Abstract

Background and objectives There is a shortage of kidneys for transplant, and many patients on the deceased donor kidney transplant waiting list would likely benefit from kidneys that are currently being discarded. In the United States, the most common reason given for discarding kidneys retrieved for transplant is procurement biopsy results. This study aimed to compare biopsy results from discarded kidneys with discard attributed to biopsy findings, with biopsy results from comparable kidneys that were successfully transplanted.

Design, setting, participants, & measurements In this retrospective, observational, case-control study, biopsy reports were examined from 83 kidneys discarded in 2010 due to biopsy findings (cases), 83 contralateral transplanted kidneys from the same donor (contralateral controls), and 83 deceased donors randomly matched to cases by donor risk profile (randomly matched controls). A second procurement biopsy was obtained in 64 of 332 kidneys (19.3%).

Results The quality of biopsy reports was low, with amounts of tubular atrophy, interstitial inflammation, arteriolar hyalinosis, and acute tubular necrosis often not indicated; 69% were wedge biopsies and 94% used frozen tissue. The correlation between first and second procurement biopsies was poor; only 25% of the variability (R^2) in glomerulosclerosis was explained by biopsies being from the same kidney. The percentages of glomerulosclerosis overlapped substantially between cases, contralateral controls, and randomly matched controls: 17.1%±15.3%, 9.0%±6.6%, and 5.0%±5.9%, respectively. Of all biopsy findings, only glomerulosclerosis>20% was independently correlated with discard (cases versus contralateral controls; odds ratio, 15.09; 95% confidence interval, 2.47 to 92.41; P=0.003), suggesting that only this biopsy result was used in acceptance decisions. One-year graft survival was 79.5% and 90.7% in contralateral and randomly matched controls, respectively, versus 91.6% among all deceased donor transplants in the Scientific Registry of Transplant Recipients.

Conclusions Routine use of biopsies could lead to unnecessary kidney discards.

Clin J Am Soc Nephrol 9: 562–571, 2014. doi: 10.2215/CJN.07610713

Introduction

There is a shortage of kidneys for transplant, and many patients on the deceased donor kidney transplant waiting list would likely benefit from kidneys that are currently being discarded. In the United States, a donor kidney biopsy is obtained from more than half of all deceased donors, and the biopsy finding is the most common reason given for discarding a kidney recovered for transplant (1).

There are reasons to suspect that routine procurement biopsies may cause more harm than good (2). The quality of procurement biopsies is likely low. Even if the quality were improved to the level of implantation biopsies, the biopsy results may not be reliable enough to predict transplant outcomes and justify decisions regarding kidney acceptance.

The purpose of this study was to compare biopsy results from discarded kidneys with discard attributed to biopsy findings, with biopsy results from comparable kidneys that were successfully transplanted. We hypothesized that the quality of procurement kidney biopsy reports used in acceptance decisions is low, the percentage of globally sclerotic glomeruli is the predominant biopsy finding used in acceptance decisions, and the extent of overlap in the biopsy results between discarded kidneys and transplanted kidneys is sufficient to call into question the utility of procurement biopsies in acceptance decisions.

Materials and Methods

Patient Protections

This was a joint study of the Organ Procurement and Transplantation Network (OPTN) and the Scientific Registry of Transplant Recipients (SRTR). Approvals were obtained from the US Department of Health and Human Services Health Resources and Services Administration (HRSA). No identifiable patient information was released to investigators outside of OPTN and SRTR.

Study Design

In this retrospective, observational, case-control study, we included all kidneys discarded in 2010 with available biopsy reports and biopsy findings indicated as the reason for discard (cases), and contralateral kidneys that also had biopsy reports but were transplanted (contralateral controls). In addition, each case was matched by donor risk to another donor from whom at least one kidney was transplanted and whose kidneys were not discarded due solely to biopsy results (randomly matched controls). Thus, there were three study groups: cases, contralateral controls, and randomly matched controls. Cases included kidneys discarded due to biopsy results. Contralateral controls included contralateral kidneys for cases that also underwent biopsy but were transplanted. Randomly matched controls included kidneys from donors matched to cases, both of which were biopsied but not discarded due to the biopsy; matching was based on kidney donor risk index, Public Health Services high-risk status, and hepatitis C virus serology.

Randomly matched controls were matched to cases by identifying the donor kidneys transplanted in the same year (2010) with the same Public Health Services high-risk status (yes or no) and hepatitis C virus serology status (positive or negative), and the most similar kidney donor risk index. The kidney donor risk index is a summary measure of the graft failure risk associated with a particular donor relative to a reference donor (3). The kidney donor profile index is a transformation of the kidney donor risk index into a percentile (0%–100%) based on a recent pool of donors (http://transplantpro.org/kdpi-calculator-available-on-unet-march-26/). A higher kidney donor profile index indicates a higher risk of graft failure. Kidneys that were discarded because of the biopsy findings or with no biopsy report available were excluded from the control sampling population, and kidneys that were discarded for reasons other than biopsy findings were not excluded.

Data Collection

We used data from OPTN and SRTR to characterize deceased donor kidneys from 2010 and to analyze graft and patient survival for transplanted kidneys. The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of OPTN, and has been described elsewhere (4). HRSA provides oversight of the activities of the OPTN and SRTR contractors.

Biopsy reports and anatomic information from cases and controls were obtained from DonorNet. Anatomic information included the following: aortic plaque (0, none; 1, mild; 2, moderate; 3, severe; or not available [NA]); renal artery plaque (0, none; 1, mild; 2, moderate; 3, severe; or NA); presence of one or more renal cysts; presence of a capsular tear, hematoma, or both; and abnormal gross appearance of the kidney (yes, no, include free-text comments). Biopsy information included the following: biopsy type wedge or needle, or NA; frozen versus paraffin-embedded tissue; number of glomeruli; number of globally sclerotic glomeruli; whether percentage of globally sclerotic glomeruli was estimated; interstitial fibrosis (0, none, 0%–5%; 1, mild, 6%–25%; 2, moderate, 26%–50%; 3, severe, >50%; or NA); interstitial inflammation (≤5%; 1, mild, 6%–25%; 2, moderate, 26%–50%; 3, severe, >50%; or NA); tubular atrophy (0, none; 1, mild, <25% of tubules; 2, moderate, 26%–50%; 3, severe, >50%; or NA); chronic arterial changes (0, none; 1, mild, <25% narrowing; 2, moderate, 26%–50%; 3, severe, >50%; or NA); arteriolar hyalinosis (0, none; 1, mild; 2, moderate; 3, severe; or NA); and acute tubular necrosis (0, none; 1, mild; 2, moderate; 3, severe; or NA).

Statistical Analyses

Comparisons of cases with the two distinct control groups (contralateral controls and randomly matched controls) were made separately. For each comparison, only pairs with known results from the case and control kidneys were included in the analysis. When we compared binary biopsy findings in cases with their contralateral controls, Mantel–Haenszel odds ratios and Wald 95% confidence intervals (95% CIs) were derived from conditional logistic regression for matched-pairs data. When we compared continuous/ordinal biopsy findings, the Hodges–Lehmann estimator of the pseudo-median difference between cases and controls (5) was estimated, and differences were compared using the Wilcoxon signed rank test for matched-pairs data. When we compared cases with randomly matched controls, analyses were modified to account for the clustering of control kidneys within donors. Binary biopsy findings were compared using Mantel–Haenszel odds ratios and Wald 95% CIs derived from conditional logistic regression for matched-pairs data with adjustment for kidney laterality. Conditional/ordinal outcomes were compared using the signed rank test for clustered data on the matched case-control differences (6). To compare binary biopsy findings from first and second biopsies from the same kidney, odds ratios were estimated from logistic regression for repeated measures using generalized estimating equations taking into account the nested correlation induced by kidney laterality within donor. Continuous/ordinal outcomes from first/second biopsies of the same kidney were compared using the signed rank test for clustered data on the matched case-control differences (6). Graft and patient survival differences between contralateral and randomly matched controls were examined using Cox proportional hazards analysis. All analyses were carried out with SAS 9.1.3 (SAS Institute, Inc., Cary, NC) and R 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria) software.

Results

Donors and Biopsies

Of the 7241 deceased kidney donors in 2010 (Figure 1), two kidneys were transplanted from 5594 deceased kidney donors (77.3%), no kidneys were transplanted from 1067 deceased kidney donors (14.7%), and one kidney was transplanted from 580 deceased kidney donors (8.0%). Of the 580 donors from whom only one kidney was transplanted, one kidney was discarded from 525 donors and the second kidney was not recovered from 55 donors. Of the 525 donors from whom one kidney was transplanted and one discarded, the discard was due to reasons other than biopsy findings for 420 donors (80.0%) and to biopsy findings for 105 donors (20%). Of these 105 donors, biopsy

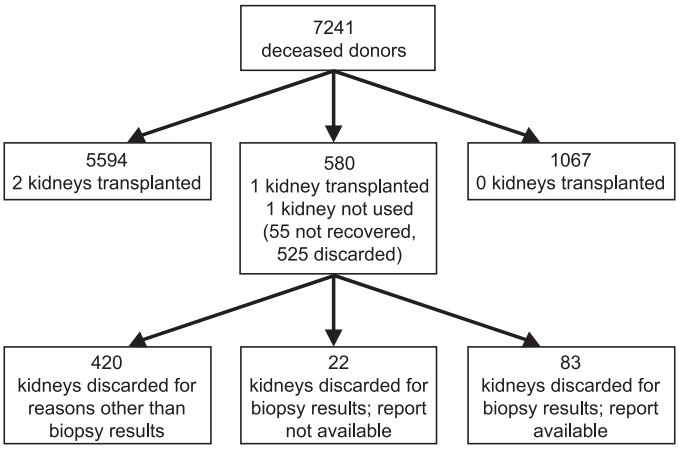

Figure 1. | **Study population selection.** The figure shows the disposition of kidneys from United States deceased donors in 2010 and their relation to the 83 discarded kidneys in this study.

reports were unavailable for 22 donors (21%) and were available (for both kidneys) for 83 donors (79%).

Thus, 83 kidneys discarded due to biopsy findings (cases) and 83 contralateral transplanted kidneys with biopsy reports (contralateral controls) were available for study. The 83 cases were matched by donor risk profile to 83 deceased donors (randomly matched controls), and 151 kidneys from these controls were transplanted. The kidney donor profile index for the 83 randomly matched control donors was virtually identical to the kidney donor profile index for cases (76.8%±17.7%; 95% CI, 72.9% to 80.7%). Fifteen kidneys were discarded from randomly matched controls with biopsy not the sole reason for discard.

First and Second Procurement Biopsies of the Same Kidney

Of the 332 kidneys studied, two biopsies of the same kidney occurred in 64 kidneys (19.3%): 24 of 83 kidneys (29%) in cases, 16 of 83 kidneys (19%) in contralateral controls, and 24 of 166 kidneys (14%) in randomly matched controls (P=0.02 by the chi-squared test). The reason for obtaining a second biopsy was usually not indicated in the records. In some instances, obtaining a second biopsy may have been routine practice for the accepting organ procurement organization. In other instances, the first biopsy may have shown moderate to severe damage and a second biopsy was obtained to confirm that this was not due to sampling error. The second biopsy was more likely to be a needle core than a wedge biopsy (Table 1, Supplemental Table 1), likely reflecting an effort to obtain better tissue sampling. The second biopsy tended to show greater chronic tubule-interstitial damage than the first biopsy; the second biopsy showed more tubular atrophy and interstitial fibrosis. The percentage of globally sclerotic glomeruli was numerically greater in the first than in the second biopsy, but this difference was not statistically significant (Figure 2, Table 1). The linear trend line equation was First Biopsy=0.4933×Second Biopsy+6.1434; R^2=0.2532; P<0.001; indicating that only 25% of the variability in glomerulosclerosis was explained by biopsies being from the same kidney. For subsequent analyses, the second biopsy was used.

Biopsy Results and Anatomic Abnormalities from Discarded Kidneys Compared with Controls

Of 332 biopsies, 12 biopsies (3.6%) showed <10 glomeruli, 51 biopsies (15.4%) showed 10–24 glomeruli, 122 biopsies (36.8%) showed 25–49 glomeruli, and 147 biopsies (44.3%) showed ≥50 glomeruli. There were no differences between cases and controls in the numbers of glomeruli in the biopsies (Tables 2 and 3, Supplemental Tables 2 and 3). The percentage of globally sclerotic glomeruli was reported in all cases and contralateral controls, and in all but two randomly matched control kidneys. Only 2 cases (2.4%), 3 contralateral controls (3.6%), and 12 randomly matched controls (7.2%) did not include a comment in the report regarding the amount of interstitial fibrosis (cases versus randomly matched controls, P=0.08). However, a description of the amount of chronic vascular damage was missing in 6 cases (7.2%), 8 contralateral controls (9.6%), and 29 randomly matched controls (17.5%) (cases versus randomly matched controls, P=0.01). The amounts of tubular atrophy, interstitial inflammation, arteriolar hyalinosis, and acute tubular necrosis were often not indicated in the biopsy report (Tables 2 and 3).

Cases showed more glomerular sclerosis than contralateral or randomly matched controls (P<0.001) (Tables 2 and 3). However, there was substantial overlap in the percentage of global glomerular sclerosis between cases and controls (Figure 3). In general, histologic differences between cases and contralateral controls (Table 2) were less than differences between cases and randomly matched controls (Table 3).

Few anatomic abnormalities that would have precluded transplant were noted in the records (Tables 4 and 5, Supplemental Tables 4 and 5). There were no differences between cases and controls in descriptions of aortic and renal artery atherosclerosis. One or more renal cysts were noted more often in cases than in contralateral or randomly matched controls. Overall, fewer cases than contralateral or randomly matched controls were noted to be anatomically normal (Tables 4 and 5).

Independent Histologic and Anatomic Correlates of Discard

We analyzed biopsy results from cases and contralateral controls to determine which factors may have led to the

Table 1. Comparison of two biopsies from the same kidney

Biopsy Characteristic	First Biopsy (n=64)	Second Biopsy (n=64)	P Value[a]
Wedge (versus needle)	40/48 (83.3)	10/48 (20.8)	<0.001
Frozen tissue (versus paraffin-embedded tissue)	37/39 (94.9)	37/39 (94.9)	NE
Number of glomeruli assessed	53.8±28.4	49.7±40.0	0.81
Percentage of global sclerosis	11.5±10.7	11.0±10.9	0.84
Biopsy findings, if reported[b]			
Tubular atrophy (36 pairs)	0.61±0.73	1.03±0.29	0.01
Interstitial fibrosis (62 pairs)	0.68±0.70	1.02±0.42	0.01
Interstitial inflammation (3 pairs)	1.00±0.00	0.33±0.58	NE
Vascular damage (55 pairs)	0.91±0.82	1.11±0.50	0.19
Arteriolar hyalinosis (3 pairs)	0.33±0.58	0.33±0.58	NE
Acute tubular necrosis (7 pairs)	0.29±0.49	0.29±0.49	NE
Missing biopsy information			
Wedge versus needle biopsy	11/64 (17.2)	5/64 (7.8)	0.14
Tissue processing method not indicated	23/64 (35.9)	4/64 (6.3)	<0.001
Tubular atrophy	23/64 (35.9)	8/64 (12.5)	0.003
Interstitial fibrosis	2/64 (3.1)	0/64 (0.0)	NE
Interstitial inflammation	32/64 (50.0)	57/64 (89.1)	<0.001
Vascular damage	7/64 (10.9)	2/64 (3.1)	0.11
Arteriolar hyalinosis	39/64 (60.9)	54/64 (84.4)	0.01
Acute tubular necrosis	48/64 (75.0)	49/64 (76.6)	0.81

Data are presented as the fraction (%) or mean±SD. NE, not estimable due to too few discordant pairings.
[a]P values for binary data were generated from logistic regression for repeated measures using generalized estimating equations and taking into account the nested correlation induced by kidney laterality within donor (5). P values for parametric data were generated from a signed rank test on the matched case-control differences for clustered data (6). See Supplemental Table 1 for details.
[b]0, none; 1, mild; 2, moderate; 3, severe.

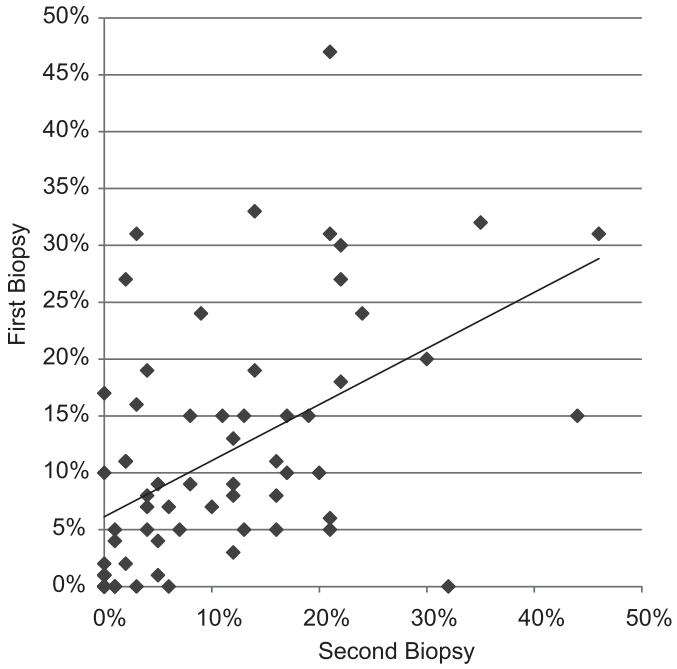

Figure 2. | Comparison of the percentage of globally sclerotic glomeruli in two biopsies from the same kidney. The figure shows the percentage of globally sclerotic glomeruli in first and second biopsies from 64 kidneys that underwent two biopsies. The linear trend equation was First Biopsy=0.4933×Second Biopsy+6.1434; R^2=0.2532; P<0.001.

decision to discard one kidney but not the other. Only a percentage of global glomerular sclerosis>20% was associated with the decision to discard based on biopsy findings (Table 6).

Transplant Outcomes

Unadjusted Kaplan–Meier graft survival was lower in recipients of contralateral control kidneys than in recipients of randomly matched control kidneys (Figure 4). One-

Table 2. Comparison of biopsies from discarded and paired control kidneys from the same donor

Biopsy Characteristic	Kidney Discarded for Biopsy Findings (n=83)	Contralateral Kidney Not Discarded (n=83)	P Value[a]
Wedge (versus needle)	42/63 (66.7)	47/63 (74.6)	0.10
Frozen tissue (versus paraffin-embedded tissue)	49/50 (98.0)	49/50 (98.0)	NE
Number of glomeruli assessed	53.5±40.9	55.2±39.8	0.50
Percentage of global sclerosis	17.1±15.3	9.0±6.6	<0.001
Percentage of global sclerosis >20%	27/83 (32.5)	4/83 (4.8)	<0.001
Biopsy findings, if reported[b]			
Tubular atrophy (52 pairs)	1.00±0.56	0.87±0.49	0.08
Interstitial fibrosis (80 pairs)	0.95±0.55	0.78±0.57	0.01
Interstitial inflammation (37 pairs)	0.81±0.57	0.65±0.54	0.07
Vascular damage (75 pairs)	1.01±0.73	0.87±0.62	0.04
Arteriolar hyalinosis (35 pairs)	0.63±0.60	0.69±0.72	NE
Acute tubular necrosis (32 pairs)	0.72±0.81	0.69±0.64	0.85
Missing biopsy information			
Wedge versus needle biopsy	18/83 (21.7)	17/83 (20.5)	0.66
Tissue processing method not indicated	29/83 (34.9)	32/83 (38.6)	0.22
Tubular atrophy	27/83 (32.5)	29/83 (34.9)	0.42
Interstitial fibrosis	2/83 (2.4)	3/83 (3.6)	NE
Interstitial inflammation	43/83 (51.8)	39/83 (47.0)	0.22
Vascular damage	6/83 (7.2)	8/83 (9.6)	NE
Arteriolar hyalinosis	44/83 (53.0)	44/83 (53.0)	1.00
Acute tubular necrosis	47/83 (56.6)	50/83 (60.2)	0.22

Data are presented as the fraction (%) or mean±SD. NE, not estimable due to too few discordant pairings.
[a]P values for binary data were generated from logistic regression for repeated measures using generalized estimating equations and taking into account the nested correlation induced by kidney laterality within donor (5). P values for parametric data were generated from a signed rank test on the matched case-control differences for clustered data (6). See Supplemental Table 2 for details.
[b]0, none; 1, mild; 2, moderate; 3, severe.

year graft survival was 79.5% and 90.7% in contralateral and randomly matched control kidneys, respectively. The unadjusted relative risk of graft failure in contralateral control kidneys compared with randomly matched control kidneys was 1.98 (95% CI, 1.12 to 3.52), and the relative risk adjusted for recipient age, sex, race, and kidney donor risk index was 2.06 (95% CI, 1.14 to 3.72). One-year patient survival was 89.2% and 97.4% in contralateral and randomly matched control kidneys, respectively (Figure 4). The unadjusted relative risk of death in contralateral compared with randomly matched control kidneys was 2.54 (95% CI, 1.12 to 5.74), and the relative risk adjusted for recipient age, sex, race, and kidney donor risk index was 2.76 (95% CI, 1.20 to 6.78).

Among recipients with functioning grafts at 12 months after transplant, the estimated GFR, estimated by the Chronic Kidney Disease Epidemiology Collaboration equation (7), was 50.0±23.1 ml/min per 1.73 m^2 in contralateral control kidneys (n=68) and 51.4±20.7 ml/min per 1.73 m^2 in randomly matched control kidneys (n=139) (P=0.67). At 12 months, 7 acute rejection episodes had occurred in recipients of contralateral control kidneys (all biopsy confirmed) and 12 had occurred in recipients of randomly matched control kidneys (11 biopsy confirmed).

Discussion

Due to the shortage of deceased donor kidneys, it is critical that kidneys suitable for transplant not be discarded unnecessarily. In 2011, 2587 kidneys retrieved for transplant in the United States were subsequently discarded (1). Of these, 966 kidneys (37.3%) were discarded due to biopsy findings, the most common reason for discard. In 2012, 50.4% of deceased donor kidneys removed for transplant underwent a procurement biopsy (personal communication, D.E.S., based on OPTN data as of March 1, 2013).

A large number of studies have examined how well kidney biopsy findings correlate with post-transplant outcomes. Most single-center studies have examined "implantation" biopsies obtained at the time of transplant surgery (8–40). These biopsies have usually been paraffin embedded, carefully stained, and interpreted by renal pathologists. Different scoring systems have been used to assess the amount of chronic damage (11,15,23,27,29,32,33,39,40). Morphometry has also been used to determine the amount of chronic damage in the transplanted kidney as accurately as possible (23,25,32). Nevertheless, these studies have generally failed to show strong correlations between histologic findings of implantation biopsies and kidney graft survival.

Although there are exceptions (41), most studies of procurement biopsies have analyzed the limited data collected in registries (42–45). Often, the only information available in registry studies is the percentage of globally sclerotic glomeruli. Like studies of implantation biopsies, studies examining the association of procurement biopsy findings with post-transplant outcomes have produced conflicting results (41–44).

Unlike implantation biopsies obtained under optimal conditions, procurement biopsies are generally obtained using frozen sections that are often interpreted by a general pathologist without special training in reading kidney

Table 3. Comparison of biopsies from discarded kidneys and randomly matched controls

Biopsy Characteristic	Kidney Discarded for Biopsy Findings (n=83)	Randomly Matched Control (n=166)	P Value[a]
Wedge (versus needle)	34/51 (66.7)	72/101 (71.3)	0.55
Frozen tissue (versus paraffin-embedded tissue)	32/33 (97.0)	57/65 (87.7)	NE
Number of glomeruli assessed (164 pairs)	53.8±41.1	51.4±32.9	0.86
Percentage of global sclerosis (164 pairs)	17.1±15.4	5.0±5.9	<0.001
Percentage of global sclerosis >20%	27/83 (32.5)	5/166 (3.0)	<0.001
Biopsy findings, if reported[b]			
Tubular atrophy (80 pairs)	1.07±0.47	0.60±0.54	<0.001
Interstitial fibrosis (150 pairs)	0.97±0.52	0.54±0.56	<0.001
Interstitial inflammation (38 pairs)	0.75±0.55	0.45±0.50	0.04
Vascular damage (127 pairs)	1.05±0.76	0.64±0.63	0.001
Arteriolar hyalinosis (24 pairs)	0.38±0.51	0.58±0.65	0.51
Acute tubular necrosis (18 pairs)	0.78±0.97	0.28±0.46	0.22
Missing biopsy information			
Wedge versus needle biopsy	18/83 (21.7)	38/166 (22.9)	0.79
Tissue processing method not indicated	29/83 (34.9)	64/166 (38.6)	0.51
Tubular atrophy	27/83 (32.5)	51/166 (30.7)	0.72
Interstitial fibrosis	2/83 (2.4)	12/166 (7.2)	0.08
Interstitial inflammation	43/83 (51.8)	85/166 (51.2)	0.92
Vascular damage	6/83 (7.2)	29/166 (17.5)	0.01
Arteriolar hyalinosis	44/83 (53.0)	99/166 (59.6)	0.27
Acute tubular necrosis	47/83 (56.6)	119/166 (71.7)	0.01

Data are presented as the fraction (%) or mean±SD. NE, not estimable due to too few discordant pairings.
[a]P values for binary data were generated from logistic regression for repeated measures using generalized estimating equations and taking into account the nested correlation induced by kidney laterality within donor (5). P values for parametric data were generated from a signed rank test on the matched case-control differences for clustered data (6). See Supplemental Table 3 for details.
[b]0, none; 1, mild; 2, moderate; 3, severe.

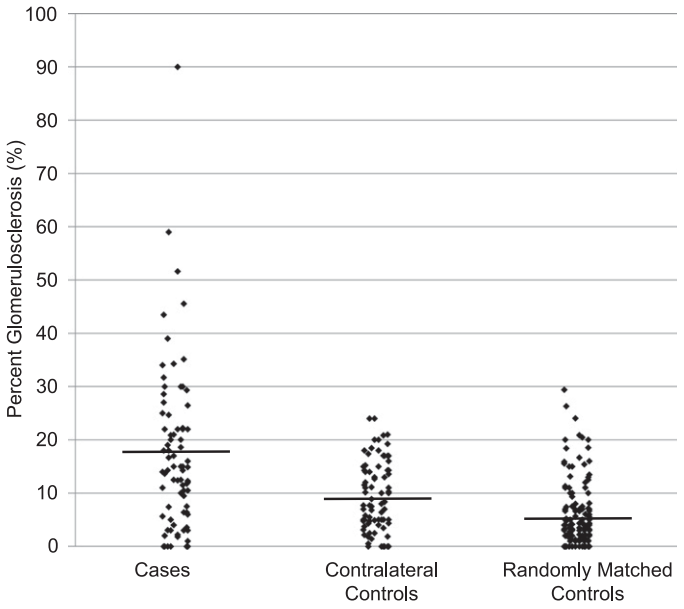

Figure 3. | Percentage of globally sclerotic glomeruli in discarded kidneys (cases), transplanted contralateral kidneys from the same donor (contralateral controls), and randomly matched controls. Horizontal lines indicate group means: 17.0%, 9.0%, and 5.0% for cases, contralateral controls, and randomly matched controls, respectively. P<0.001 for cases versus contralateral controls and for cases versus randomly matched controls.

biopsies. The results may be reported to a surgeon not trained in renal pathology, who then must decide whether to accept the kidney for a particular patient.

We found that the quality of biopsy reports used in acceptance decisions was poor. Most biopsies were wedge biopsies; studies have shown that core needle biopsies are

Table 4. Comparison of anatomic abnormalities from discarded and paired control kidneys from the same donor

Biopsy Characteristic	Kidney Discarded for Biopsy Findings (*n*=83)	Randomly Matched Control (*n*=166)	*P* Value[a]
Aortic plaque (49 pairs)[b]	1.49±1.14	1.45±1.12	NE
Aortic plaque not mentioned	32/83 (38.6)	28/83 (33.7)	0.18
Renal artery plaque (55 pairs)[b]	0.75±0.99	0.75±1.02	1.00
Renal artery plaque not mentioned	26/83 (31.3)	24/83 (28.9)	0.42
Cysts noted	27/83 (32.5)	18/83 (21.7)	0.05
Capsular tear/hematoma noted	2/83 (2.4)	2/83 (2.4)	1.00
Normal, no anatomic abnormalities	29/83 (34.9)	37/83 (44.6)	0.05

Data are presented as the fraction (%) or mean±SD. NE, not estimable due to too few discordant pairings.
[a]*P* values for binary data were generated from logistic regression for repeated measures using generalized estimating equations and taking into account the nested correlation induced by kidney laterality within donor (5). *P* values for parametric data were generated from a signed rank test on the matched case-control differences for clustered data (6). See Supplemental Table 4 for details.
[b]0, none; 1, mild; 2, moderate; 3, severe.

Table 5. Comparison of anatomic abnormalities from discarded kidneys and randomly matched controls

Biopsy Characteristic	Kidney Discarded for Biopsy Findings (*n*=83)	Randomly Matched Control (*n*=166)	*P* Value[a]
Aortic plaque (61 pairs)[b]	1.37±1.29	1.30±1.01	0.93
Aortic plaque not mentioned	32/83 (38.6)	64/166 (33.6)	0.99
Renal artery plaque (78 pairs)[b]	0.63±0.86	0.82±1.05	0.61
Renal artery plaque not mentioned	26/83 (31.3)	57/166 (34.3)	0.56
Cysts noted	27/83 (32.5)	22/166 (13.3)	<0.001
Capsular tear/hematoma noted	2/83 (2.4)	3/166 (1.8)	0.75
Normal, no anatomic abnormalities	29/83 (34.9)	91/166 (54.8)	0.001

Data are presented as the fraction (%) or mean±SD.
[a]*P* values for binary data were generated from logistic regression for repeated measures using generalized estimating equations and taking into account the nested correlation induced by kidney laterality within donor (5). *P* values for parametric data were generated from a signed rank test on the matched case-control differences for clustered data (6). See Supplemental Table 5 for details.
[b]0, none; 1, mild; 2, moderate; 3, severe.

Table 6. Independent correlates of discard among 166 kidneys retrieved from 83 deceased donors

Percentage of Glomerulosclerosis	Discarded Kidney (*n*=83)	Contralateral Kidney (*n*=83)	Conditional Odds Ratio for Discard	*P* Value[a]
0.0	8 (9.6)	10 (12.1)	Reference	–
0.1–5.0 (*n*=35)	12 (14.5)	23 (27.7)	0.93 (0.22 to 3.89)	0.92
5.1–10.0 (*n*=25)	8 (9.6)	17 (20.5)	1.03 (0.22 to 4.78)	0.97
10.1–20.0 (*n*=57)	28 (33.7)	29 (34.9)	2.42 (0.56 to 10.44)	0.23
>20.0 (*n*=31)	27 (32.5)	4 (4.8)	15.09 (2.47 to 92.41)	0.003

Data are presented as *n* (%) or odds ratio (95% confidence interval).
[a]*P* values were generated from a signed rank test on the matched case–control differences for clustered data (6).

superior to wedge biopsies (46,47). Almost all biopsies were processed using frozen tissue. The number of glomeruli is often used as an indicator of biopsy adequacy, and Wang *et al.* found that biopsies with at least 25 glomeruli were better predictors of graft survival (13). In this study, 63 of 332 biopsies (19%) showed <25 glomeruli and only 146 of 332 (43.9%) showed ≥50. At least 90% of biopsies reported the amount of interstitial fibrosis and chronic arterial damage (Tables 2 and 3), but one-third did not mention chronic tubular atrophy, and half did not comment on the presence or absence of arteriolar hyalinosis or the amount of interstitial inflammation. Two-thirds of biopsies failed to comment on the presence, absence, or severity of acute tubular necrosis.

A comparison of two biopsies from the same kidney demonstrated significant differences (Table 1), calling into

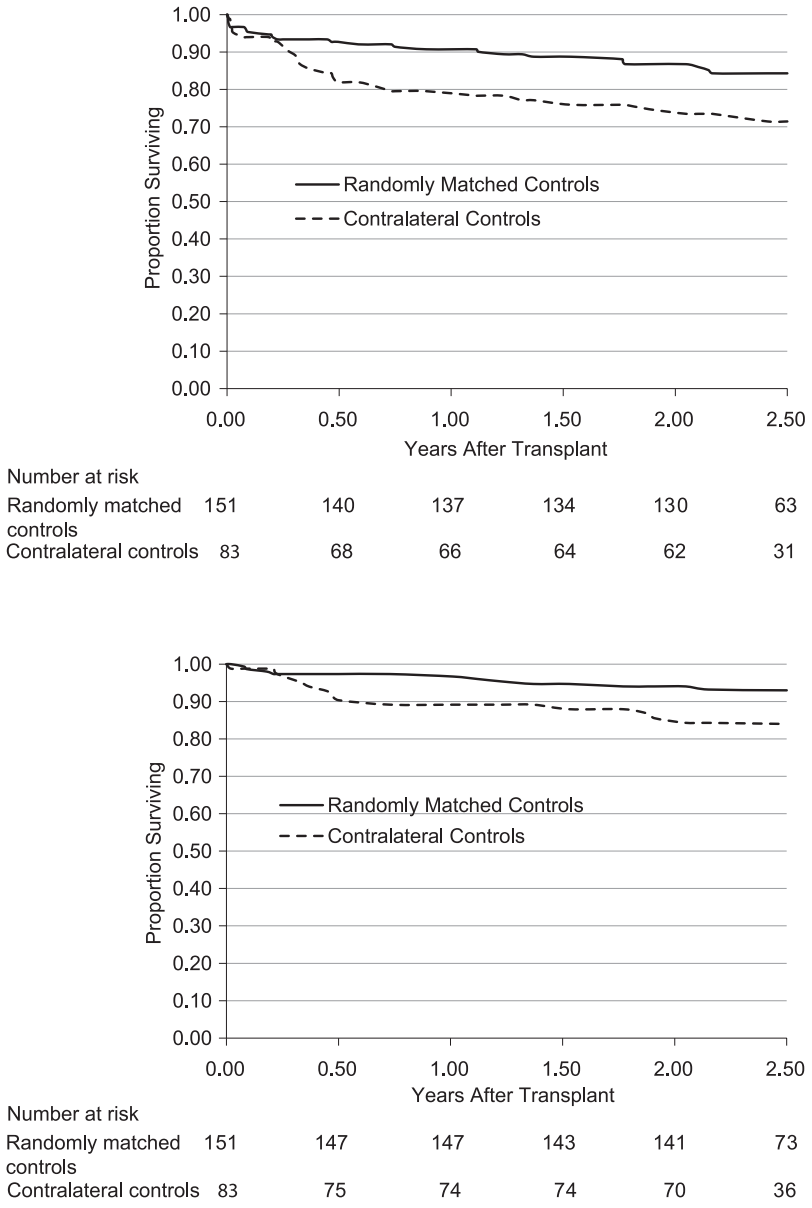

Figure 4. | Graft (top) and patient (bottom) survival for recipients of contralateral control kidneys and randomly matched control kidneys. Unadjusted Kaplan–Meier survival curves are shown.

question the reliability of biopsies for making acceptance decisions. Notably, the percentage of glomerulosclerosis in the 64 pairs of biopsies from the same kidney was substantially discordant (Figure 2).

The most important findings in this study are the overlap in biopsy findings between kidneys that were discarded and kidneys that were transplanted, and that glomerulosclerosis≥20% was the only biopsy finding independently predictive of discard. To the best of our knowledge, ours is the first controlled study to compare biopsy findings between discarded kidneys and matched transplanted kidneys. Although the difference in the percentage of globally sclerotic glomeruli was statistically significant, there was substantial overlap between groups (Figure 3). Glomerulosclerosis>20% is often used as a marker of severe chronic kidney damage. This tradition can be traced to a very small study of implantation biopsies published in 1995 (10). In the present study, 32.5% of discarded kidneys were reported to have >20% glomerulosclerosis (Table 2). Similarly, there was substantial overlap, albeit with some statistically significant differences, in most other histologic parameters between cases and controls (Tables 2 and 3).

Graft survival of kidneys contralateral to kidneys that had been discarded due to biopsy findings was worse than graft survival of deceased donor kidneys with a comparable kidney donor risk index (Figure 4). Rates of acute rejection were low in both control groups. Among recipients with functioning grafts at 12 months, estimated GFR was approximately 50 ml/min per 1.73 m^2. A 1-year graft survival of 80%, compared with 91.6% for all deceased donor recipients in the United States in 2010 (1), may be acceptable for many patients.

There are important caveats to this study. The biopsies from discarded kidneys that were contralateral to the transplanted kidneys may not represent all biopsies from discarded kidneys. It is also possible that the quality of biopsies and their utility could be improved. However, numerous studies have shown poor correlation of implantation biopsies with transplant outcomes, despite these implantation biopsies being performed under optimal conditions.

A reasonable conclusion from this and other studies is that the widespread practice of routinely obtaining procurement biopsies should be abandoned, as has been successfully done in Europe (2). If abandoning routine procurement biopsies is not acceptable in the United States, then perhaps a randomized controlled trial could be designed to more precisely determine the benefits and harms of procurement biopsies. In such a trial, the quality of procurement biopsies could be maximized by using needle rather than wedge biopsies, obtaining three adequate cores, requiring at least 25 glomeruli in the biopsy for it to be considered adequate, replacing frozen tissue with rapid paraffin embedding whenever possible, and using a standardized reporting form to encourage adequate reporting of all important biopsy elements.

In summary, the results of this study suggest that the information obtained from procurement biopsies is of low quality and may lead to unnecessary discard of transplantable kidneys. The practice of obtaining routine procurement biopsies should either be abandoned or more critically reexamined in appropriately designed clinical trials.

Acknowledgments

The authors thank SRTR colleagues Delaney Berrini for manuscript preparation, and Nan Booth, MPH, ELS, for manuscript editing.

This work was conducted under the auspices of the Minneapolis Medical Research Foundation, contractor for SRTR, as a deliverable under Contract HHSH250201000018C (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation) and the United Network for Organ Sharing (UNOS), contractor for OPTN, under Contract 234-2005-370011C. As a US Government–sponsored work, there are no restrictions on its use. The views expressed herein are those of the authors and not necessarily those of the US Government, UNOS, or OPTN.

Disclosures

None.

References

1. Matas AJ, Smith JM, Skeans MA, Lamb KE, Gustafson SK, Samana CJ, Stewart DE, Snyder JJ, Israni AK, Kasiske BL: OPTN/SRTR 2011 Annual Data Report: Kidney. *Am J Transplant* 13[Suppl 1]: 11–46, 2013
2. Hopfer H, Kemény E: Assessment of donor biopsies. *Curr Opin Organ Transplant* 18: 306–312, 2013
3. Rao PS, Schaubel DE, Guidinger MK, Andreoni KA, Wolfe RA, Merion RM, Port FK, Sung RS: A comprehensive risk quantification score for deceased donor kidneys: The kidney donor risk index. *Transplantation* 88: 231–236, 2009
4. Leppke S, Leighton T, Zaun D, Chen SC, Skeans M, Israni AK, Snyder JJ, Kasiske BL: Scientific Registry of Transplant Recipients: Collecting, analyzing, and reporting data on transplantation in the United States. *Transplant Rev (Orlando)* 27: 50–56, 2013
5. Hollander M, Wolfe DA: Nonparametric Statistical Methods, 2nd Ed., New York, John Wiley & Sons, 1999
6. Datta S, Satten GA: A signed-rank test for clustered data. *Biometrics* 64: 501–507, 2008
7. Inker LA, Eckfeldt J, Levey AS, Leiendecker-Foster C, Rynders G, Manzi J, Waheed S, Coresh J: Expressing the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) cystatin C equations for estimating GFR with standardized serum cystatin C values. *Am J Kidney Dis* 58: 682–684, 2011
8. Leunissen KM, Bosman FT, Nieman FH, Kootstra G, Vromen MA, Noordzij TC, van Hooff JP: Amplification of the nephrotoxic effect of cyclosporine by preexistent chronic histological lesions in the kidney. *Transplantation* 48: 590–593, 1989
9. Taub HC, Greenstein SM, Lerner SE, Schechner R, Tellis VA: Reassessment of the value of post-vascularization biopsy performed at renal transplantation: The effects of arteriosclerosis. *J Urol* 151: 575–577, 1994
10. 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
11. Minakawa R, Tydén G, Lindholm B, Reinholt FP: Donor kidney vasculopathy: Impact on outcome in kidney transplantation. *Transpl Immunol* 4: 309–312, 1996
12. Szánya J, Szakály P, Magyarlaki T, Balogh Z, Nagy J, Nagy KK: Predictive morphological findings in "zero-hour" biopsies of renal allografts. *Acta Chir Hung* 36: 346–348, 1997
13. Wang HJ, Kjellstrand CM, Cockfield SM, Solez K: On the influence of sample size on the prognostic accuracy and reproducibility of renal transplant biopsy. *Nephrol Dial Transplant* 13: 165–172, 1998
14. Cosyns JP, Malaise J, Hanique G, Mourad M, Baldi A, Goebbels RM, Squifflet JP: Lesions in donor kidneys: Nature, incidence, and influence on graft function. *Transpl Int* 11: 22–27, 1998
15. Lehtonen SR, Taskinen EI, Isoniemi HM: Histopathological findings in renal allografts at time of transplantation and correlation with onset of graft function. *APMIS* 107: 945–950, 1999
16. Oda A, Morozumi K, Uchida K: Histological factors of 1-h biopsy influencing the delayed renal function and outcome in cadaveric renal allografts. *Clin Transplant* 13[Suppl 1]: 6–12, 1999
17. Oberbauer R, Rohrmoser M, Regele H, Mühlbacher F, Mayer G: Apoptosis of tubular epithelial cells in donor kidney biopsies predicts early renal allograft function. *J Am Soc Nephrol* 10: 2006–2013, 1999
18. Kuypers DR, Chapman JR, O'Connell PJ, Allen RD, Nankivell BJ: Predictors of renal transplant histology at three months. *Transplantation* 67: 1222–1230, 1999
19. Lu AD, Desai D, Myers BD, Dafoe DC, Alfrey EJ: Severe glomerular sclerosis is not associated with poor outcome after kidney transplantation. *Am J Surg* 180: 470–474, 2000
20. 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
21. Di Paolo S, Stallone G, Schena A, Infante B, Gesualdo L, Paolo Schena F: Hypertension is an independent predictor of delayed graft function and worse renal function only in kidneys with chronic pathological lesions. *Transplantation* 73: 623–627, 2002
22. Escofet X, Osman H, Griffiths DF, Woydag S, Adam Jurewicz W: The presence of glomerular sclerosis at time zero has a significant impact on function after cadaveric renal transplantation. *Transplantation* 75: 344–346, 2003
23. Howie AJ, Ferreira MA, Lipkin GW, Adu D: Measurement of chronic damage in the donor kidney and graft survival. *Transplantation* 77: 1058–1065, 2004
24. Ortiz F, Paavonen T, Törnroth T, Koskinen P, Finne P, Salmela K, Kyllönen L, Grönhagen-Riska C, Honkanen E: Predictors of renal allograft histologic damage progression. *J Am Soc Nephrol* 16: 817–824, 2005
25. Lopes JA, Moreso F, Riera L, Carrera M, Ibernon M, Fulladosa X, Grinyó JM, Serón D: Evaluation of pre-implantation kidney biopsies: Comparison of Banff criteria to a morphometric approach. *Kidney Int* 67: 1595–1600, 2005
26. Ugarte R, Kraus E, Montgomery RA, Burdick JF, Ratner L, Haas M, Hawxby AM, Karp SJ: Excellent outcomes after transplantation of

deceased donor kidneys with high terminal creatinine and mild pathologic lesions. *Transplantation* 80: 794–800, 2005
27. Re L, Cicora F, Petroni J, Goldberg J, Rial MC, Casadei D: Comparison between clinical and histopathological scoring in cadaveric kidney transplantation and its correlation with posttransplant evolution. *Transplant Proc* 38: 903–904, 2006
28. Arias LF, Blanco J, Sanchez-Fructuoso A, Prats D, Duque E, Sáiz-Pardo M, Ruiz J, Barrientos A: Histologic assessment of donor kidneys and graft outcome: Multivariate analyses. *Transplant Proc* 39: 1368–1370, 2007
29. Ibernon M, González-Segura C, Moreso F, Gomà M, Serón D, Fulladosa X, Torras J, Garcia-Huete L, Gil-Vernet S, Cruzado JM, Carrera M, Duarte V, Grinyó JM: Donor structural and functional parameters are independent predictors of renal function at 3 months. *Transplant Proc* 39: 2095–2098, 2007
30. 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
31. Carroll RP, Macgregor L, Walker RG: The improvement in survival of expanded criteria donor kidneys with transplantation era. *Clin Transplant* 22: 324–332, 2008
32. Munivenkatappa RB, Schweitzer EJ, Papadimitriou JC, Drachenberg CB, Thom KA, Perencevich EN, Haririan A, Rasetto F, Cooper M, Campos L, Barth RN, Bartlett ST, Philosophe B: The Maryland aggregate pathology index: A deceased donor kidney biopsy scoring system for predicting graft failure. *Am J Transplant* 8: 2316–2324, 2008
33. Anglicheau D, Loupy A, Lefaucheur C, Pessione F, Létourneau I, Côté I, Gaha K, Noël LH, Patey N, Droz D, Martinez F, Zuber J, Glotz D, Thervet E, Legendre C: A simple clinico-histopathological composite scoring system is highly predictive of graft outcomes in marginal donors. *Am J Transplant* 8: 2325–2334, 2008
34. Matignon M, Desvaux D, Noël LH, Roudot-Thoraval F, Thervet E, Audard V, Dahan K, Lang P, Grimbert P: Arteriolar hyalinization predicts delayed graft function in deceased donor renal transplantation. *Transplantation* 86: 1002–1005, 2008
35. Koppelstaetter C, Schratzberger G, Perco P, Hofer J, Mark W, Ollinger R, Oberbauer R, Schwarz C, Mitterbauer C, Kainz A, Karkoszka H, Wiecek A, Mayer B, Mayer G: Markers of cellular senescence in zero hour biopsies predict outcome in renal transplantation. *Aging Cell* 7: 491–497, 2008
36. Wazna E, Pazik J, Perkowska-Ptasińska A, Lewandowski Z, Nazarewski S, Chmura A, Durlik M: Arteriolar hyalinization in implantation kidney biopsies as a predictor of graft function. *Transplant Proc* 41: 2975–2977, 2009
37. Cockfield SM, Moore RB, Todd G, Solez K, Gourishankar S: The prognostic utility of deceased donor implantation biopsy in determining function and graft survival after kidney transplantation. *Transplantation* 89: 559–566, 2010
38. Sulikowski T, Tejchman K, Ziętek Z, Urasińska E, Domański L, Sieńko J, Romanowski M, Safranow K, Zukowski M, Ciechanowicz A, Ciechanowski K, Ostrowski M: Histopathologic evaluation of pretransplantation biopsy as a factor influencing graft function after kidney transplantation in 3-year observation. *Transplant Proc* 42: 3375–3381, 2010
39. Lin NC, Yang AH, King KL, Wu TH, Yang WC, Loong CC: Results of kidney transplantation from high-terminal creatinine donors and the role of time-zero biopsy. *Transplant Proc* 42: 3382–3386, 2010
40. Navarro MD, López-Andréu M, Rodríguez-Benot A, Ortega-Salas R, Morales ML, López-Rubio F, García PA: Significance of preimplantation analysis of kidney biopsies from expanded criteria donors in long-term outcome. *Transplantation* 91: 432–439, 2011
41. 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
42. Edwards EB, Posner MP, Maluf DG, Kauffman HM: Reasons for non-use of recovered kidneys: The effect of donor glomerulosclerosis and creatinine clearance on graft survival. *Transplantation* 77: 1411–1415, 2004
43. Cicciarelli J, Cho Y, Mateo R, El-Shahawy M, Iwaki Y, Selby R: Renal biopsy donor group: The influence of glomerulosclerosis on transplant outcomes. *Transplant Proc* 37: 712–713, 2005
44. Bajwa M, Cho YW, Pham PT, Shah T, Danovitch G, Wilkinson A, Bunnapradist S: Donor biopsy and kidney transplant outcomes: An analysis using the Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) database. *Transplantation* 84: 1399–1405, 2007
45. 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
46. Haas M, Segev DL, Racusen LC, Bagnasco SM, Melancon JK, Tan M, Kraus ES, Rabb H, Ugarte RM, Burdick JF, Montgomery RA: Arteriosclerosis in kidneys from healthy live donors: Comparison of wedge and needle core perioperative biopsies. *Arch Pathol Lab Med* 132: 37–42, 2008
47. Mazzucco G, Magnani C, Fortunato M, Todesco A, Monga G: The reliability of pre-transplant donor renal biopsies (PTDB) in predicting the kidney state. A comparative single-centre study on 154 untransplanted kidneys. *Nephrol Dial Transplant* 25: 3401–3408, 2010

Received: July 18, 2013 **Accepted:** October 23, 2013

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

This article contains supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.07610713/-/DCSupplemental.

See related editorial, "Procurement Biopsies in Kidneys Retrieved for Transplantation," on pages 443–444.