ORIGINAL ARTICLE

Association between procurement biopsy findings and deceased donor kidney outcomes: a paired kidney analysis

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SUMMARY

Unfavourable procurement biopsy findings are the most common reason for deceased donor kidney discard in the United States. We sought to assess the association between biopsy findings and post-transplant outcomes when donor characteristics are accounted for. We used registry data to identify 1566 deceased donors of 3132 transplanted kidneys (2015–2020) with discordant right/left procurement biopsy classification and performed time-to-event analyses to determine the association between optimal histology and hazard of death-censored graft failure or death. We then repeated all analyses using a local cohort of 147 donors of kidney pairs with detailed procurement histology data available (2006–2016). Among transplanted kidney pairs in the national cohort, there were no significant differences in incidence of delayed graft function or primary nonfunction. Time to death-censored graft failure was not significantly different between recipients of optimal versus suboptimal kidneys. Results were similar in analyses using the local cohort. Regarding recipient survival, analysis of the national, but not local, cohort showed optimal kidneys were associated with a lower hazard of death (adjusted HR 0.68, 95% CI 0.52–0.90, $P = 0.006$). In conclusion, in a large national cohort of deceased donor kidney pairs with discordant right/left procurement biopsy findings, we found no association between histology and death-censored graft survival.

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Key words
deceased donor kidney transplant, organ donor procurement kidney biopsy, transplant outcomes

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Introduction

Although kidney transplantation is associated with better survival and quality of life compared to dialysis in patients with end-stage kidney disease, transplantation in the United States is constrained by the limited availability of organs [1–5]. In spite of this shortage, one out of every five deceased donor kidneys recovered for the purpose of transplantation is instead discarded [6]. The most frequently cited reason for deceased donor kidney discard is unfavourable findings on procurement biopsies – typically the presence of chronic scarring (nephrosclerosis) [6–9]. Findings from these biopsies, performed during the allocation process to assess organ quality, account for 38% of kidney discards in the United States [6,10].

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Despite this reliance on procurement biopsies, their reliability, reproducibility and association with post-transplant outcomes have been repeatedly called into question [10]. Multiple procurement biopsies performed on the same kidney very often yield discrepant results, and findings on these biopsies do not approximate findings on gold standard biopsies performed after implantation [11–14]. Further, although procurement biopsy findings may be associated with post-transplant outcomes in unadjusted analyses, nephrosclerosis on these biopsies is not associated with graft longevity after accounting for donor characteristics already available during allocation such as age and comorbidities [10,15–22]. However, these studies have been limited by selection biases, as kidneys with procurement biopsies showing more severe nephrosclerosis are less likely to be transplanted.

Given that most deceased donors have two kidneys recovered and that histological patterns in both kidneys in an individual would be expected to be consistent, kidney pairs from a given donor that have different procurement biopsy findings can help us determine the utility of procurement biopsy findings when donor characteristics are held constant. Using a primary cohort and validation cohort that consist of pairs of kidneys from the same donor that each underwent a biopsy but were reported to have discordant procurement biopsy findings, we attempted to study the relationship between histological findings and graft longevity. We hypothesized that there would be no difference in post-transplant outcomes between kidneys in these pairs.

Materials and methods

Part 1: national cohort

Using data from the Organ Procurement and Transplantation STAR (Standard Transplant Analysis and Research) file, we identified all deceased kidney donors with information recorded on procurement biopsy regarding glomerulosclerosis, interstitial fibrosis and tubular atrophy, and vascular disease for both right and left kidneys (n = 24 091 donors with complete bilateral kidney procurement biopsy reports). Given that these data were not captured before 2015, our analysis was limited to donors with kidneys recovered between 1/1/2015 and 3/16/2020. After excluding donors who did not have two kidneys recovered for transplantation (either because only one kidney was recovered or one kidney was recovered with the express intent of use for research) and donors who had both kidneys discarded, a cohort of 17 630 donors, among whom 1951 (11%) had kidneys with discordant procurement biopsy histology [defined below], was identified (Fig. S1). After excluding donors with unilateral discards and those who had at least one kidney used in a multi-organ transplant, or who had at least one kidney used in a transplant that had missing data (number of HLA mismatches or recipient follow-up status), we were left with a final cohort of 1566 donors of 3132 kidneys for this part of the analysis (Fig. S1).

Biopsy scores were analysed as they are recorded in the data set (Table S1). 'Optimal' procurement biopsy histology for any kidney was defined as a score of 1 for all biopsy components (glomerulosclerosis, interstitial fibrosis and tubular atrophy and vascular disease), whereas a score of ≥2 for any component led to organ classification as 'suboptimal'. Discordant pairs were defined as kidney pairs from the same donor in which one kidney was classified as suboptimal and the other was classified as optimal.

Part 2: local cohort

Given the lack of granularity in the national procurement biopsy data including which procurement biopsy results were reported in the case of sequential biopsies and the treatment of procurement biopsy results reported in ranges, we repeated the analysis using a continuous retrospective cohort of all deceased donor kidneys transplanted at Columbia University Medical Center from 1/1/2006 to 12/31/2016 that had ≥1 procurement biopsy (n = 1049; Fig. S2) using a scoring system we have previously studied [14]. We excluded kidneys with missing biopsy reports (n = 6) or follow-up data (n = 1), and those transplanted as part of multi-organ transplants (n = 31), yielding a cohort of 1011 eligible kidneys transplanted at our centre with procurement biopsy results. Review of donor information indicated this cohort reflected 860 unique donors, of whom 769 had two kidneys that were recovered for the purpose of transplantation. Among these 760 donors, 194 (25%) had kidneys with discordant procurement biopsy histology. After excluding donors for whom one kidney was discarded, we were left with a final cohort of 147 donors of 294 kidneys for this part of the analysis (Fig. S2); none of these had missing data for any variables included in outcomes analyses.

Biopsy details for both of each donor's kidneys were manually extracted directly from the individual biopsy reports available in DonorNet®. Information regarding glomerulosclerosis, interstitial fibrosis and tubular

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atrophy (IFTA) and vascular disease as reported by the interpreting pathologists was obtained for each biopsy directly from procurement biopsy histology reports. Given a lack of standardization in the identification of specific types of vascular disease (e.g. arteriosclerosis, arteriolosclerosis and hyalinosis) in procurement biopsy reports, vascular disease was identified generally as the degree of whichever chronic vascular changes were reported.

We assigned a score of 0 (most favourable) to 3 (least favourable) for each histological compartment based on the thresholds outlined in Table S1, consistent with prior analyses using this cohort [11,13,14]. In cases where a range of values was reported for a given compartment, the lower end of the range was used to assign the histological score (ex. vascular disease 'mild to moderate' was scored as 1). 'Optimal' histology on a given biopsy was defined as having a score ≤1 for all three biopsy compartments, whereas 'suboptimal' histology was defined as a score of ≥2 for at least one compartment. In cases where the kidney's biopsy report was missing information for one of the biopsy compartments, histology was considered optimal if each of the remaining compartments had a score ≤1. In cases where more than one procurement biopsy was reported for any kidney, only the results of the first procurement biopsy were included in the analysis.

Statistical analysis

All donor, recipient and transplant variables were included as recorded in the STAR file. Recipients were classified having pre-emptive transplants if they were recorded as not receiving dialysis prior to transplant, and no pre-transplant dialysis date was recorded. Recipients were classified as having high panel reactive antibody (PRA) if any reported PRA value (initial, peak or last) was ≥80%. In all other cases, including those with all PRA values <80% and those with no PRA values recorded, recipients were classified as not having high PRA.

Chi-squared and Wilcoxon rank sum tests were first used to compare characteristics of donors whose kidney pairs had discordant versus concordant histology.

The remainder of the analyses were then restricted to transplants performed using kidneys from donors with discordant pairs (one suboptimal, one optimal) that were both transplanted. Recipient and transplant characteristics for transplants using suboptimal versus optimal kidneys from there pairs were compared using chi-squared and Wilcoxon rank sum tests. The proportion of recipients requiring dialysis in the first week after transplant and the proportion of transplants experiencing primary graft nonfunction (defined as graft failure within 90 days of transplantation) were compared using chi-squared and Fischer's exact tests where appropriate.

Unadjusted death-censored graft survival analysis and patient survival analysis were performed using the Kaplan–Meier method. We performed univariate and multivariable time-to-event analyses for death-censored graft failure and patient survival using Cox proportional hazards models. Multivariable analyses were adjusted for recipient age, recipient sex, recipient race (white versus not white), recipient diabetes status (diabetes versus no diabetes), recipient dialysis time (as a continuous variable, with time of 0 for pre-emptive transplants), recipient high PRA status (yes versus no), number of human leukocyte antigen (HLA) mismatches and transplant cold ischaemia time. Patients who were lost to follow-up were censored on the last date of follow-up reported.

All analyses were performed separately for the national and local cohorts. Analyses were performed using STATA MP 15 (Stata Corp, College Station, TX, USA). Statistical significance was identified by a two-sided $\alpha < 0.05$. This study was approved by the Columbia University Medical Center Institutional Review Board. All clinical and research activities associated with this study were consistent with the principles of the Declaration of Istanbul.

Results

National cohort: donors with discordant versus concordant bilateral kidney histology

We identified 17 630 United States deceased donors (1/1/2015–3/16/2020) who had two kidneys recovered for the purpose of transplantation that both had complete procurement biopsy information available (Fig. S1). Among these, 1951 (11%) had kidney pairs with discordant optimal and suboptimal histology. Donors of kidney pairs with discordant histology had no differences in age, sex, history of diabetes, history of hypertension or kidney donor risk index compared to donors with concordant histology between their kidneys (Table 1). Small differences in race (73% vs. 69% White race, $P = 0.001$) and final donor creatinine (median 1.0 vs. 1.1 mg/dl, $P = 0.002$) were statistically significant but were of unclear clinical significance. In both groups, 83% of donors had both kidneys transplanted, while 17% had one kidney discarded.

Table 1. Characteristics of United States deceased kidney donors with concordant versus discordant bilateral kidney procurement biopsy histology.

Median (IQR) or *n* (column %)	All (*n* = 17 630; 100%)	Discordant (*n* = 1951, 11%)	Concordant (*n* = 15 679, 89%)	*P*
Age (years)	48 (37–56)	48 (37–56)	48 (37–56)	0.34
Female	7131 (40)	825 (42)	6306 (40)	0.08
White race	12 202 (69)	1417 (73)	10 785 (69)	0.001
History of diabetes	2193 (12)	233 (12)	1960 (13)	0.48
History of hypertension	7603 (43)	841 (43)	6762 (43)	0.99
Final creatinine (mg/dl)	1.1 (0.8–1.8)	1.0 (0.7–1.7)	1.1 (0.8–1.9)	0.002
Kidney donor risk index	1.39 (1.16–1.67)	1.40 (1.16–1.66)	1.39 (1.15–1.67)	0.43
Both kidneys transplanted	14 643 (83)	1624 (83)	13 019 (83)	0.82

National cohort: outcomes using a suboptimal versus optimal kidney from a discordant pair

Among transplanted kidney pairs from the same donor that had discordant procurement biopsy histology (one kidney suboptimal, one kidney optimal), there were no differences in any recipient demographic or medical characteristics (age, sex, race, diabetes, pre-emptive transplant status, dialysis time, prior organ transplant or high PRA status), number of transplant HLA mismatches, or transplant cold ischaemia time (Table 2). Suboptimal histology designation in these pairs was predominantly due to the presence of mild nephrosclerosis. Among suboptimal kidneys, only 5% had moderate or severe glomerulosclerosis and only 1% each had moderate or severe IFTA or vascular disease (Table S2). Early post-transplant outcomes of requiring dialysis within the first week after transplant (35% of transplants using optimal kidneys, 37% of transplants using suboptimal kidneys) and primary graft nonfunction (2% for each group) were also similar for recipients of suboptimal versus optimal kidneys (Table 2).

In time-to-event analysis, time to death-censored graft failure for optimal kidneys from discordant pairs was not significantly different from that of suboptimal kidneys in unadjusted analysis [hazard ratio (HR) 0.90, 95% CI 0.66–1.24, $P = 0.52$; Fig. 1) or after adjusting for recipient and transplant characteristics (adjusted HR 0.90, 95% CI 0.66–1.24, $P = 0.52$; Table 3). However, recipients of optimal kidneys had a lower hazard of death in both unadjusted (HR 0.68, 95% CI 0.52–0.89, $P = 0.005$; Fig. 1) and adjusted (adjusted HR 0.68, 95% CI 0.52–0.90, $P = 0.006$) analyses (Table 3).

Local cohort: donors with discordant versus concordant bilateral kidney histology

We next identified 769 deceased donors who had two kidneys recovered for the purpose of transplantation that both had procurement biopsy information available, of which at least one was transplanted at our centre between 2006 and 2016 (Fig. S2). Among these donors, 194 (25%) had kidney pairs with discordant histology and 575 (75%) had pairs with concordant histology. Donors with discordant pairs had lower median final creatinine (1.1 mg/dl vs. 1.5 mg/dl, $P < 0.001$) but otherwise, there were no discernible differences between groups (Table 4). Right and left kidney biopsies were interpreted by the same pathologist for each pair.

Table 2. Recipient and transplant characteristics for kidney pairs included in the analysis.

Median (IQR) or *n* (column %)	Suboptimal kidney recipient *n* = 1566, 50%	Optimal kidney recipient *n* = 1566, 50%	*P*
Recipient characteristics			
Age, years	58 (49–65)	57 (48–65)	0.29
Female	611 (39)	588 (38)	0.40
White	639 (41)	590 (38)	0.07
Diabetes	662 (42)	637 (41)	0.37
High PRA (PRA ≥80%)	215 (14)	244 (16)	0.14
Pre-emptive transplant	120 (8)	129 (8)	0.55
Dialysis time, years (if not pre-emptive)	4.3 (2.4–6.3)	4.4 (2.3–6.7)	0.22
Prior organ transplant	157 (10)	166 (11)	0.60
Estimated post-transplant survival (%)	60 (33–82)	58 (32–80)	0.19
Transplant characteristics			
Cold ischaemia time, h	18.4 (13.4–24.3)	18.1 (13.0–23.8)	0.17
HLA mismatches	4 (3–5)	4 (3–5)	0.88
Transplant outcomes			
Required dialysis in week 1	587 (37)	546 (35)	0.13
Primary nonfunction	35 (2)	25 (2)	0.19

HLA, human leukocyte antigen; PRA, panel reactive antibody.

Local cohort: outcomes using a suboptimal versus optimal kidney from a discordant pair

Recipient characteristics were similar for transplanted suboptimal versus optimal kidneys from discordant pairs (Table 5) with the exception of median pre-transplant dialysis time that was lower among non-pre-emptive recipients of suboptimal versus optimal kidneys (2.4 vs. 3.3 years, $P = 0.02$). Cold ischaemia time at transplant was similar for both groups. Suboptimal histology designation was mostly attributable to moderate or severe glomerulosclerosis, and 40% of suboptimal kidneys had >25% glomerulosclerosis (Table S3). However, 3% and 18% of suboptimal kidneys had moderate IFTA or vascular disease, respectively, and no kidneys had severe IFTA or vascular disease.

There was no difference in the need for dialysis in the first post-transplant week between groups. Of note, the four cases of primary graft nonfunction all occurred among transplants using suboptimal kidneys (Table 5).

In time-to-event analysis limited to this cohort, death-censored graft failure of optimal kidneys from discordant pairs was not significantly different compared to suboptimal kidneys either in unadjusted (HR 0.90, 95% CI 0.56–1.44, $P = 0.66$; Fig. 2) or adjusted analyses (adjusted HR 0.88, 95% CI 0.54–1.45, $P = 0.63$; Table 6). Unlike in the national cohort, transplantation using optimal kidneys did not appear to be protective against mortality following a transplant with a suboptimal kidney either in unadjusted analyses (HR 0.93, 95% CI 0.60–1.45, $P = 0.75$; Fig. S2) or after adjusting for recipient and transplant characteristics (HR 0.91, 95% CI 0.58–1.44, $P = 0.69$; Table 6).

Discussion

Despite the fact that the demand for kidney transplantation greatly exceeds the number of kidneys available and that even less than ideal deceased donor kidneys provide a survival advantage, 20% of recovered deceased donor kidneys are discarded in the United States [6]. Further, the overwhelming majority of even those that are used for transplantation are declined on behalf of at least one recipient [6,23,24]. Concerns about organ quality are the most common reasons the deceased donor kidneys are not utilized for transplantation, despite the fact that many of the measures of quality that are associated with kidney discard are not actually associated with inferior post-transplant outcomes [6,8,25–28]. Understanding the most appropriate ways to use available assessments of organ quality and their limitations is essential to improving organ utilization. Herein, we present an analysis of kidney pairs with shared donors but discordant procurement biopsy histological classification and demonstrate that optimal procurement biopsy histology was not associated with better death-censored graft survival. This finding adds to the growing body of literature indicating that procurement biopsy findings do not appear to provide additional prognostic value beyond what can already be ascertained from other donor parameters including clinical history.

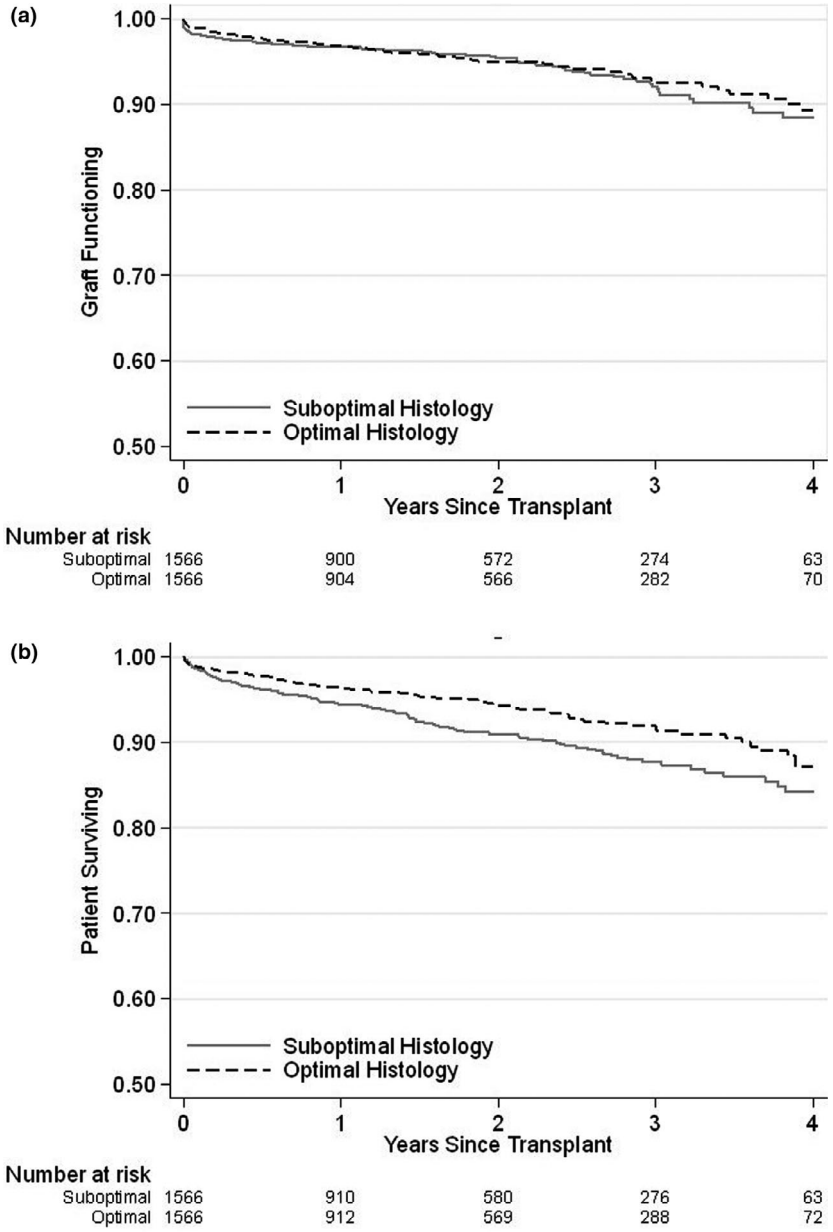

Figure 1 Unadjusted Kaplan–Meier curves of (a) death-censored graft survival and (b) patient survival based on transplantation with optimal versus suboptimal kidney from discordant pair.

By comparing groups of kidney pairs from the same donor, our analysis demonstrates that procurement biopsies do not provide additional reliable reproducible information to help predict post-transplant graft survival. This underscores earlier concerns regarding procurement biopsy reproducibility that were noted using analyses that identified sequential procurement biopsies performed on the same kidney as being discrepant [11]. Not surprisingly, procurement biopsy findings are also frequently dissimilar to findings on gold standard reperfusion biopsies performed after kidney implantation [13]. The limitations of procurement biopsies, which should ostensibly provide objective information about organ quality, have been attributed to factors including oversampling of subcapsular tissue when wedge biopsies are performed, inferior tissue processing and staining for frozen section specimens compared to gold standard formalin-fixed and paraffin embedded biopsies, and time pressured interpretation by pathologists who often lack expertise in kidney pathology [10,13,15,16,29–31].

The earliest studies demonstrating an association between nephrosclerosis found on deceased donor

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Table 3. Association between transplantation with optimal versus suboptimal kidney from discordant pair and post-transplant outcomes.

		Unadjusted			Adjusted		
	Failures	HR	95% CI	*P*	HR	95% CI	*P*
Death-censored graft failure							
Optimal histology (vs. suboptimal)	156	0.90	0.66–1.24	0.52	0.90	0.66–1.24	0.52
Patient survival							
Optimal histology (vs. suboptimal)	215	0.68	0.52–0.89	0.005	0.68	0.52–0.90	0.006

Adjusted models are adjusted for recipient age, sex, race (white versus not white), diabetes status (diabetes versus no diabetes), dialysis time, high panel reactive antibody [PRA] status (PRA ≥80% vs. PRA <80%), number of human leukocyte antigen mismatches and transplant cold ischaemia time.

Table 4. Characteristics of donors with concordant versus discordant bilateral kidney histology, among donors whose procurement biopsy reports were manually reviewed.

Median (IQR) or *n* (column %)	All (*n* = 769, 100%)	Discordant (*n* = 194, 25%)	Concordant (*n* = 575, 75%)	*P*
Age (years)	48 (37–54)	48 (36–54)	48 (37–54)	0.58
Female	329 (43)	86 (44)	243 (42)	0.61
White race	279 (36)	63 (32)	216 (38)	0.20
History of diabetes	116 (15)	36 (19)	80 (14)	0.12
History of hypertension	37 (44)	79 (41)	258 (45)	0.31
Final creatinine (mg/dl)	1.4 (0.9–2.4)	1.1 (0.8–1.8)	1.5 (0.9–2.6)	<0.001
Kidney donor risk index	1.40 (1.14–1.70)	1.39 (1.10–1.66)	1.40 (1.15–1.71)	0.27
Both kidneys transplanted	591 (77)	147 (76)	444 (77)	0.68

Table 5. Recipient and transplant characteristics for kidney pairs whose donor procurement biopsies reports were manually reviewed.

Median (IQR) or *n* (column %)	Suboptimal kidney recipient *n* = 147, 50%	Optimal kidney recipient *n* = 147, 50%	*P*
Recipient characteristics			
Age, years	58 (47–64)	57 (46–65)	0.86
Female	70 (48)	58 (39)	0.16
White	65 (44)	62 (42)	0.72
Diabetes	56 (38)	49 (33)	0.39
High PRA (PRA ≥80%)	13 (9)	14 (10)	0.84
Pre-emptive transplant	18 (12)	22 (15)	0.46
Dialysis time, years (if not pre-emptive)	2.4 (<0.1–4.4)	3.3 (1.6–5.2)	0.02
Prior organ transplant	26 (18)	24 (16)	0.10
Transplant characteristics			
Cold ischaemia time, h	29.7 (18.3–38.0)	30 (20.7–37.0)	0.89
HLA mismatches	5 (4–5)	4 (4–5)	0.14
Transplant outcomes			
Required dialysis in week 1	67 (46)	59 (40)	0.35
Primary nonfunction	4 (2)	0 (0)	0.12*

HLA, human leukocyte antigen; PRA, panel reactive antibody.

*Fischer's exact test performed.

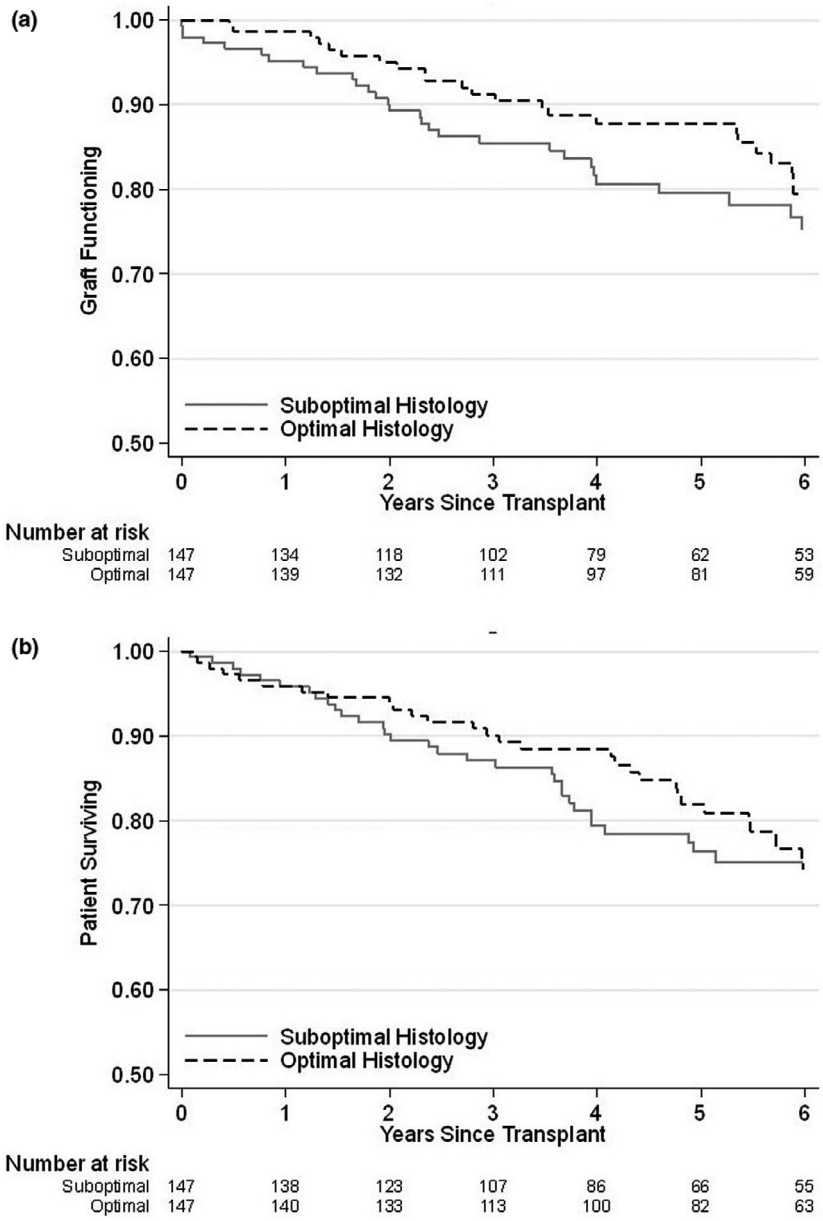

Figure 2 Unadjusted Kaplan–Meier curves of (a) death-censored graft survival and (b) patient survival based on transplantation with optimal versus suboptimal kidney from discordant pair, among kidney transplants whose donor procurement biopsies reports were manually reviewed.

kidney procurement biopsies and inferior post-transplant outcomes were followed by multiple studies demonstrating that these associations are no longer present once donor demographics and medical history are taken into account [10,15–22]. In particular, glomerulosclerosis and nephron loss seen on these biopsies may largely be attributable to donor age and reflect normal age-related senescence rather than underlying pathophysiology [29,32–35]. These concerns are consistent with our findings from kidney pairs that procurement biopsy findings do not predict graft survival when donor characteristics are accounted for. Further, the fact that we identified this quantity of kidney pairs from the same donor with discordant histology in the current study is itself an indication that sampling error and processing limitations lead to procurement biopsy findings that do not necessarily reflect organ quality. It is also possible that pathologist training and experience affect the reliability and prognostic ability of procurement biopsy findings [10]. Although we lack information about the pathologists who interpreted the biopsies in the national cohort, right and left kidneys in each pair in the local cohort were read by the same pathologist.

Table 6. Association between transplantation with optimal versus suboptimal kidney from discordant pair and post-transplant outcomes, among kidney transplants whose donor procurement biopsies reports were manually reviewed.

	Unadjusted			Adjusted		
	HR	95% CI	*P*	HR	95% CI	*P*
Death-censored graft failure						
Optimal histology (vs. suboptimal)	0.90	0.56–1.44	0.66	0.88	0.54–1.45	0.63
Patient survival						
Optimal histology (vs. suboptimal)	0.93	0.60–1.45	0.75	0.91	0.58–1.44	0.69

Adjusted models are adjusted for recipient age, sex, race (white versus not white), diabetes status (diabetes versus no diabetes), dialysis time, high panel reactive antibody [PRA] status (PRA ≥80% vs. PRA <80%), number of human leukocyte antigen mismatches and cold ischaemia time.

Alternatively, it remains possible that true differences in chronic renal parenchymal scarring within kidneys pairs included in our cohort explain their discrepant biopsy findings. However, significant asymmetric nephrosclerosis due to systemic factors such as age and medical comorbidities has not been described. Although factors such as unilateral renal artery stenosis could theoretically lead to asymmetric nephrosclerosis, we believe it is unlikely that this finding contributes to the right–left differences we observed given that a majority of donors in our study did not have diabetes or hypertension and the use allografts from donors with severe renal artery stenosis is rare. Rather, the fact that kidneys with optimal and suboptimal procurement histology had similar death-censored graft failure suggests that differences in procurement biopsy results reflect sampling variation rather than differences in nephrosclerosis.

Given the limited value of these biopsies, reducing the reliance on procurement biopsies during deceased donor kidney allocation is a necessary step to improve organ utilization without sacrificing organ quality assessment. A recent analysis comparing kidneys discarded in the United States to histologically matched kidneys transplanted in France (where procurement biopsy findings are not used to inform allocation or organ acceptance) showed that the French kidneys had excellent outcomes, suggesting that waitlisted patients would have benefited had the discarded American kidneys been accepted for transplantation [16]. In addition to improving kidney utilization, the reduction or elimination of procurement biopsies may also improve allocation efficiency by eliminating the time and cost associated with performing, processing and interpreting these biopsies. Considering that 84% of deceased donor kidneys are declined on behalf of at least one waitlisted candidate, reducing procurement biopsy use can potentially also expedite organ placement, potentially improving graft longevity and decreasing both reduced cold ischaemia time associated injury and subsequent delayed graft function [23,36].

We should note that while we found no association between optimal procurement biopsy histology and improved death-censored graft survival in either the national or local analyses, optimal histology was associated with a significantly decreased hazard of death in the national cohort even after adjusting for recipient characteristics. Recipients of the kidneys with the suboptimal and optimal kidneys were almost indistinguishable, which suggests the possibility of residual confounding that was not measured in the dataset. For example, suboptimal kidneys are often more likely to be transplanted into recipients whose centres expect to have shorter survival based on clinical measures that are not captured in a registry, such as frailty or dialysis complicated by hypotension. Candidates with lower expected survival are known to benefit from the trade of shortened wait times associated with access to lower-quality kidneys rather than waiting for better organ offers [37,38]. Whether the recipients of kidneys with suboptimal histology either receive a different immunosuppression strategy over time and thus different risk of complications that could not be ascertained.

The absence of an association between optimal procurement biopsy histology and death-censored graft survival in both the national and local cohorts increases the veracity of our findings given that each cohort has unique strengths and limitations. The national registry includes a large, nationally representative cohort of transplants; however, biopsy data were only included beginning in 2015. In contrast, although the local cohort of manually reviewed biopsies is smaller, it includes kidneys from 2006 to 2016 and therefore has longer follow-up. Additionally, since the use of kidneys

with moderate or severe nephrosclerosis is uncommon, the local Cohort's longer study period led to the inclusion of a greater number of kidneys with more severe chronic changes, as evidenced by a greater number of suboptimal kidneys with moderate or severe glomerulosclerosis or vascular disease in the local cohort compared to the national cohort. Further, the granular data resulting from manual biopsy report review allows more systematic scoring of biopsy parameters: in the national registry, we are unable to identify procurement biopsy findings that were reported in ranges (e.g. 'moderate-to-severe' or '20–30%' IFTA) or whether procurement biopsy data reflected the first or second biopsy for kidneys for which multiple biopsies were performed. In contrast, in the local cohort, we were able to specify methods to analyse these scenarios as outlined in the Methods. Finally, the analyses of both the national and local cohort demonstrate a lack of association between histological classification and outcomes among kidney pairs using each of two different scoring systems. The scoring system for the national cohort was based on data as it is recorded in the national transplant registry, and optimal histology was assigned by the absence of chronic renal parenchymal scarring, as it is defined in clinical practice. The scoring system for the local cohort was consistent with prior procurement biopsy analyses using this cohort [11,13]. Scoring thresholds were based on biopsy report categories used by our organ procurement organization and others, and criteria for optimal versus suboptimal designation were based on our prior analyses.

Strengths of our study include the use of national registry procurement biopsy data coupled with validation of these results using more granular, manually collected biopsy data. Limitations include the likelihood of selection bias: given that only kidney pairs in which both kidneys were transplanted could be included when assessing post-transplant outcomes, unilateral discards that are likely to have resulted from discordant biopsy results would have resulted in those donor being excluded from our analysis. Accordingly, few kidneys in the national cohort had moderate or severe chronic changes in any biopsy component. However, moderate-to-severe glomerulosclerosis and vascular disease were more common in the local cohort, suggesting that our findings were not solely due to an absence of advanced nephrosclerosis in transplanted suboptimal kidneys. Given that the national data set did not include information on biopsy findings prior to 2015, this portion of the analysis was necessarily limited by relatively shorter follow-up. Additional standardization on the classification of vascular disease in procurement biopsies may also be informative, as our data lacked details regarding the presence of arteriosclerosis, arteriolosclerosis and/or hyalinosis.

In conclusion, discordant procurement biopsy histology among kidney pairs is not uncommon. Histological findings in these pairs are not associated death-censored graft survival. An association between transplantation using kidneys with optimal histology and longer patient survival was found using a national, but not a local, cohort. These findings suggest that procurement biopsies do not appear to provide additional prognostic information beyond what can already be ascertained by other donor characteristics and existing clinical information. Decreasing the use of procurement biopsies in a manner that would be consistent with other national organ allocation systems may help reduce kidney discard, allocation time and cost without reducing the accuracy of organ quality assessments by transplant centres.

Authorship

SAH: study concept and design. SAH: data analysis. SAH, KLK, SC, KN, AP and SM: interpretation of data. SAH, KLK, SC, KN, AP and SM: manuscript preparation and revision.

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Conflicts of interest

The authors declare that they have no conflicts of interest to disclose.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Procurement biopsy analysis histological classification and score for the national cohort (a) and local paired kidney cohort (b).

Table S2. Distribution of procurement biopsy results for kidneys included in the national cohort.

Table S3. Distribution of procurement biopsy results for kidneys included in the local cohort.

Figure S1. Flow diagram of study cohort.

Figure S2. Flow diagram of secondary analysis among kidneys whose donor procurement biopsies reports were manually reviewed.

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