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Variation in Use of Procurement Biopsies and Its Implications for Discard of Deceased Donor Kidneys Recovered for Transplant

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Abbreviations: aOR, adjusted odds ratio; AUC, area under the curve; CMV, cytomegalovirus; EBV, Epstein Barr virus; DGF, delayed graft function; EBE, empirical Bayes estimate; ECD, expanded criteria donor; eGFR, estimated glomerular filtration rate; GS, glomerulosclerosis; ICC, interclass correlation coefficient; HCV, hepatitis C virus; KDPI, kidney donor profile index; KDRI, kidney donor risk index; MAPI, Maryland Aggregate Pathology Index; MOR, median odds ratio; OPTN, Organ Procurement and

Transplantation Network; OPO, organ procurement organization; PHS, Public Health Service; SRTR, Scientific Registry of Transplant Recipients.

ABSTRACT

Use of procurement biopsies in deceased donor kidney acceptance is controversial. We analyzed Scientific Registry of Transplant Recipients data (*n* = 59,328 allografts, 2014-2018) to describe biopsy practices across US organ procurement organizations (OPOs) and examine relationships with discards, using hierarchical modeling to account for OPO and donor factors. Median odds ratios (MORs) provide medians of the odds that allografts with identical reported traits would be biopsied or discarded from two randomly drawn OPOs. Biopsies were obtained for 52.7% of kidneys. Biopsy use rose in a graded manner with kidney donor profile index (KDPI). Biopsy rates differed significantly among OPOs (22.8% to 77.5%), even after adjustment for KDPI and other donor factors. Discard rates also varied from 6.6% to 32.1% across OPOs. After adjustment for donor factors and OPO, biopsy was associated with more than 3 times the likelihood of discard (adjusted odds ratio ($_{95\%LCL}$aOR$_{95\%UCL}$), $_{3.29}3.51_{3.76}$). This association was most pronounced for low-risk (KDPI <20) kidneys (aOR, $_{5.45}6.47_{7.69}$), with minimal impact at KDPI >85 (aOR, $_{0.88}1.15_{1.51}$). Adjusted MORs for kidney discard and biopsy were greatest for low-risk kidneys. Reducing the rate of unnecessary biopsy and improving the accuracy of pathologic findings in higher-KDPI organs may help reduce graft discard rates.

INTRODUCTION

The ongoing shortage of organs contributes significantly to increased waitlist mortality, prolonged waiting times, and higher cost of care for patients with end-stage renal disease seeking kidney transplants.[1,2] Although the total number of deceased donors has grown nationally (albeit slowly), the waiting list remains large, with nearly 100,000 candidates. Currently, only one-third of patients undergo transplant within 5 years of listing, and many die or become too sick before receiving an organ offer.[3] Despite this critical need, and evidence that even high kidney donor risk index (KDRI) organs are beneficial for appropriate recipients,[4,5] the discard rate of recovered, potentially transplantable kidneys increased markedly during the 2000s, and remains around 20%.[6] Although the new US kidney allocation system included provisions designed to increase placement of high-risk organs,[3] the high rate of kidney discard persists, thought to reflect both changing donor demographics and transplant program concerns about program metrics and optimizing outcomes.[7]

Among factors that may be associated with increased rates of kidney discard is the decision to perform a procurement biopsy,[8] to assess the "quality" of deceased donor organs, especially those previously classified as from expanded criteria donors (ECD). The practice became more common after a 1995 report by Gaber and colleagues demonstrated an increased rate of delayed graft function (DGF) and graft failure in patients receiving grafts with >20% glomerular sclerosis.[9] Additional criteria, including the degree of inflammation, arteriolar disease, fibrosis, and tubular atrophy, are also considered important, but are not universally applied when determining whether or not to accept a donor organ.[10] Despite widespread procurement biopsy use, concern is growing about the reliability of data derived from biopsy interpretation, the majority of which is based on frozen sections. Liapis and colleagues' report from the Banff consensus conference demonstrated poor correlation in a prospective analysis of pathologic results from frozen section biopsy.[10] Except for glomerular sclerosis (GS) in wedge biopsy, correlation between renal pathologists was poor or fair for arteriolar disease, fibrosis, and hyalinosis for frozen wedge or core biopsies. Furthermore, in a systematic review, Wang et al reported poor correlation between procurement biopsy findings and clinically important outcomes including graft failure, DGF, and estimated glomerular filtration rate (eGFR).[11] Notably, routine procurement biopsies are not generally used outside of the US.[12]

Nonetheless, despite the lack of compelling data supporting use of biopsies in making decisions about the suitability of recovered kidneys for transplant, biopsy results are cited as the most common reason for organ refusal.[6] Understanding variation in biopsy practice patterns in relationship to organ quality can frame subsequent efforts to reduce variability in performance of renal biopsies by

standardizing practices that promote maximal use of available organs. The current study was designed to describe the national landscape of procurement biopsy practices across organ procurement organizations (OPOs) in the US, and to examine relationships between biopsy and kidney discard.

METHODS

Data sources

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), US Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors. We conducted a study of single kidneys recovered for the purpose of transplant. En-bloc and dual allografts were excluded. The data allow identification of left versus right kidney, pediatric en-bloc, or dual status of the organ. Details on donor characteristics, including demographic information, comorbid conditions known at the time of death, donation after circulatory death status, and other donor-risk factors were available. Information on how OPOs handled the recovery of these organs, including biopsy and discard status, was also available. Baseline demographic information ascertained for kidney transplant recipients from OPTN included age, sex, and race as reported by the transplant centers.

Sample and donor characteristics

Kidney allograft characteristics were quantified using the kidney donor risk index (KDRI), which combines a variety of donor factors to summarize risk of graft failure after kidney transplant into a composite number.[13] The KDRI expresses the relative risk of kidney graft failure for a given donor compared with the median kidney donor from last year; values exceeding 1 have higher expected risk than the median donor, and vice versa. Elements of the KDRI score include donor age, height, weight, race, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C virus (HCV) status, and donation after circulatory death. The kidney donor profile index (KDPI) is a remapping of the KDRI onto a cumulative percentage scale, such that a donor with a KDPI of 80% has higher expected risk of graft failure than 80% of all kidney donors recovered last year.[14] In addition to the components of KDPI, other donor factors identified in the national registry include: viral infection serostatus (hepatitis B core antibody status, cytomegalovirus [CMV] seropositivity, Epstein Barr Virus [EBV] seropositivity), cancer, smoking, substance use (alcohol, cocaine, other drugs), vasodilator use

prior to recovery, Public Health Service (PHS) high risk with HCV, PHS high risk without HCV, and pumped kidney.

Outcomes: Biopsies and Discards

Although common practice is to biopsy a single kidney and extrapolate results to the pair from each donor, each kidney obtained was analyzed independently for the purpose of this study. This was to allow for discordant decisions, as each kidney in the pair had different permutations and combinations of biopsy, discard, or both. Raw biopsy and discard rates were aggregated at the OPO level.

Analyses

Unadjusted Variation in Biopsy and Discard Practices across OPOs

To visually assess unadjusted variation in biopsy and discard rates across the US, the observed proportion of deceased donor kidneys that were biopsied and discarded at the OPO level were plotted. Patterns were examined overall, and for KDPI <20 and >85. National average, unadjusted discard rates by biopsy status, and KDPI strata were also examined. To assess the relationship between biopsy practice and operational efficiency, we examined associations between median cold ischemia time and rates of biopsy and discard across OPOs.

Combined OPO and Case-Level Modeling

Bi-level hierarchical models were constructed to adjust for clustering effects in kidney biopsies and in discards. Level 1 comprised donor factors, and level 2 represented the OPO. Empirical Bayes estimates (EBEs) provided the adjusted proportion (with 95% confidence intervals [CI]) of the outcome of interest (biopsy or discard), incorporating case-mix adjustment from the hierarchical model. A 95% CI for a given OPO's EBE of biopsy or discard that does not include the median national rate of use indicates a practice that is statistically significantly different from expected considering clinical factors in the model. To account for clinical factors that may explain practice variation, the models also included KDPI and other donor factors identified in the national database. Biopsy was considered in discard models as a covariate.

Heterogeneity in biopsy use and discards by OPO was quantified using median odds ratios (MOR). The MOR provides the median of the odds that a kidney from a donor with identical characteristics will undergo biopsy (or be discarded) when two OPOs are drawn at random (performed for all possible pairs of OPO). For example, a MOR of 1.5 means that if OPOs are selected at random across all OPOs, a donor with a given set of reference characteristics is, on average, 50% more likely to

undergo biopsy (or discard) at one of the randomly selected OPOs than at the other.[15] In the national model, KDPI 20%-50% was selected as the reference. Because of the clear, strong impact of KDPI on the study outcome, analyses were also stratified by KDPI level (<20%, 20%-50%, 51%-85%, >85%). In the adjustment for donor factors, the reference case was defined as absence of other known risk factors for organ discard including hepatitis B core antibody, CMV antibody, EBV antibody, and prior substance use. The adjusted odds ratio ($_{95\%\ LCL}aOR_{95\%\ UCL}$) of undergoing biopsy (or discard) for a recovered kidney was determined for KDPI level and other donor factors, after accounting for the effect of OPO differences using the hierarchical model. In the discard models, average adjusted discard rates were reported as the probability of discard adjusted for other factors within the stratum.

Data were analyzed using Stata 13, College Station, TX. Hierarchical logistic regression modeling was in Stata using the "xtmelogit" command with OPO as a random intercept. The MOR was calculated using "xtmrho" (third party suite) command.

RESULTS

Study sample

From December 2014 (date of the revised kidney allocation system) to August 2018, 61,902 deceased donor kidneys were recovered for transplant. After excluding 2008 en-bloc and 566 dual kidneys, a final cohort of 59,328 donor kidneys was available for analysis (**Table 1**). Donated organs from all 58 OPOs were included. The average biopsy rate over the period of our study across all OPOs was 52.7% (*n* = 31,272), varying substantially across OPOs, from 22.8% to 77.5% (**Figure 1A**). Over the period studied, the biopsy rate increased nationally, from 51.3% in 2014-2015 to 53.1% in 2017-2018. The average rate of discard was 18.4% (*n* = 11,538), also varying substantially, from 6.6% to 32.1%, across OPOs. The overall national rate of discard remained generally stable (2014, 19.2%, to 2018, 18.9%).

Biopsy and discard characteristics

The decision to perform a biopsy was strongly associated with established donor characteristics. We found a 5-fold increase in unadjusted biopsy rates from the lowest to highest strata of KDPI (**Figure 2; Table 1**). In the lowest-risk group (KDPI <20), 19% of kidneys were biopsied. By comparison, 95% of KDPI >85 kidneys were biopsied. Other donor characteristics not included in the KDPI that were associated with higher biopsy rates included seropositivity for hepatitis B core, CMV, or EBV; history of cancer; smoking; substance use (alcohol, cocaine, other drugs); need for vasodilators, PHS high risk with HVC seropositivity, PHS high risk without HCV, and subsequent pulsatile perfusion.

Rates of biopsy and kidney discard varied significantly between OPOs. Variation in biopsy frequency was greatest for kidneys with KDPI <20 (1.6% to 62.5%) and less for KDPI >85 kidneys (58.3% to 100%) (**Figure 1B**). As expected, the unadjusted rate of kidney discard was positively correlated with KDPI regardless of biopsy (**Figure 2**). The unadjusted discard rate was 19-fold higher (66.2% vs. 3.8%) for higher-risk (KDPI >85) than for low-risk (KDPI <20) kidneys. Discard rates varied widely by OPO within KDPI strata; some OPOs discarded only 6.8% of high-KDPI (>85) organs while others discarded 90.9% (**Figure 1C**).

The rate of biopsy was strongly correlated with median cold ischemia time at OPOs (**Figure 3A**). For each 10.7% increase in the rate of kidney biopsy, median cold ischemia time at the OPO increased by 1 hour (P<.001). However, there was no significant correlation between median cold ischemia time and discard rate (p=0.12) (**Figure 3B).**

Risk-adjusted assessment of the decision to perform a biopsy

In a hierarchical analysis adjusted for KDPI, other donor factors, and OPO, increasing KDPI level was strongly associated with procurement kidney biopsy. For example, compared with the reference group (KDPI 21-50), the adjusted odds of a biopsy were 78% lower (aOR, $_{0.21}0.22_{0.23}$) for low-risk kidneys (KDPI <20) and 21-fold higher (aOR, $_{18.88}21.36_{24.16}$) for higher-risk (KDPI >85) kidneys (**Table 2**). Other factors associated with high biopsy rates in the multivariate analysis included known history of drug, alcohol, or smoking use; prior history of cancer; hepatitis B core antibody positivity, and non-HCV-positive PHS status. In contrast, use of vasodilator therapy prior to recovery (12.1% of all donors) was associated with an 11% reduced risk of biopsy.

Factors associated with increased discard rates

Similar trends were noted when examining the relationship of discard with donor factors (**Table 2**). Compared with the reference group (KDPI 21-50), low-risk kidneys (KDPI <20) were 52% less likely to be discarded (aOR, $_{0.44}0.48_{0.53}$). High-risk kidneys (KDPI >85) were 11-fold more likely to be discarded (aOR $_{10.31}11.18_{12.12}$). Other donor factors associated with increased risk of discard were a history of smoking (aOR, $_{1.27}1.34_{1.42}$), cancer (aOR, $_{1.04}$ $1.16_{1.30}$), and PHS increased risk with HCV seropositivity (aOR $_{4.08}4.53_{5.03}$).

Relationship between kidney biopsy and organ discard

Procurement biopsy significantly increased the odds of kidney discard. Even after adjustment for KDPI and other donor factors, biopsy was associated with 3.5-fold (aOR, $_{3.29}$ $3.51_{3.76}$) increased odds of discard. When stratified by KDPI level, biopsy (vs. no biopsy) was associated with an increased rate of discard at each level (**Figure 4**). However, this effect was most pronounced for KDPI <20 kidneys (aOR, $_{5.46}6.47_{7.69}$) versus KDPI >85 kidneys (aOR, $_{0.88}1.15_{1.51}$). The association of biopsy rate and discard rate remained stable over the course of this analysis.

Variation in OPO Biopsy and Discard Practice

OPO-level practice patterns had a significant impact on the variability in biopsy rates nationally. In a null model clustering for OPO without adjusting donor characteristics, the MOR for biopsy performance was 1.57 (**Table 3**). The addition of all donor-level factors increased the MOR from 1.57 to 1.94, suggesting that variation in biopsy rate among OPOs was not explained by differences in donor characteristics. Assessment of the measures of heterogeneity by KDPI demonstrated that variation was highest among kidneys with KDPI >85 (MOR = 2.58) (**Figure 5**). However, even among low-risk kidneys, there was significant adjusted variation in biopsy use (MOR = 1.99). Together, these data indicate significant

unexplained variability in OPO biopsy practice following adjustment for multiple known donor risk characteristics.

These data also confirm the marked differences in risk-adjusted kidney discard rates between OPOs. In a null model clustering for OPO and without donor factors, the MOR for discard was 1.34 (**Table 3**). This value did not change with addition of donor factors, suggesting that OPO-level practice patterns and not donor characteristics were the major drivers of variation. The impact of biopsy practice on the adjusted risk of discard differed for lower- and higher-risk kidneys (**Table 4; Figure 6**). For KDPI 0-20 kidneys, the MOR increased from 1.31 to 1.65 when a biopsy was performed. Conversely, for higher-risk kidneys (KDPI >85), the MOR decreased with biopsy from 1.98 when no biopsy was performed to 1.74, suggesting less variation across OPO discard rates among biopsied organs, and that variation in discard rates is heavily influenced by OPO practices, organ quality, and the decision to perform a biopsy.

DISCUSSION

The decision to perform a biopsy at the time of deceased donor kidney recovery is highly variable among OPOs, ranging from 23% to 78% of organs recovered for transplant. Clearly, a portion of this disparity is driven by differences in donor characteristics, as KDPI and other donor factors correlated highly with the decision to perform a biopsy. However, even within equivalent KDPI strata, we found marked variation in the decision to perform a biopsy. This difference in practice patterns reflects decisions made by OPOs and their associated transplant programs. Significant variation was also noted in discard rates nationally, with rates nearly 5-fold higher in high-discard regions. The association between biopsy and discard was strongest for low-risk kidneys (KDPI <20%) and weakest for the highest-KDPI organs. Overall, kidney biopsy was associated with 3.5-times the likelihood of discard after controlling for other donor characteristics, indicating its importance in influencing choices regarding organ acceptance. Increased biopsy rates were also associated with markedly greater median cold ischemia times. However, there was no association between median cold ischemia time and discard rate.

The relationship between preimplantation (or time-zero) kidney biopsy results and long-term allograft outcomes has been evaluated in a variety of retrospective single-center and registry studies. Wang et al evaluated 18 studies examining the association of GS and graft failure, including both procurement and post-reperfusion biopsies, which were evaluated as frozen sections or subsequently on permanent paraffin fixed slides. In the largest study examined in the systematic review, Bajwa examined 12,129 patients in the OPTN database and found that graft survival was reduced by 5% at 5-year decrements for grafts with >5% compared with <5% GS (P <0.001).[16] However, further increases in GS above 5% did not predict worse outcome, including for grafts with >20% GS. Reports by Edwards et al. and Sung et al. using US transplant registry data found that GS >20% was not an independent risk factor for graft failure for ECD organs.[17,18] No large studies have confirmed Gaber's early report correlating GS and DGF.[9] Furthermore, the systemic review suggested that association of GS and graft function have been conflicting; two studies demonstrated lower GFR with increasing GS, while three studies failed to demonstrate this effect.[11]

The association between other pathologic findings and kidney transplant outcomes is also conflicting. In their systematic review, Wang et al reported that only 50% of studies demonstrated an association between arteriolar hyalinosis or arterial sclerosis and graft failure rates.[11] Biopsy findings were associated with reduced eGFR at 1 year in patients with severe arteriolar hyalinosis, sclerosis, or both, but not with graft failure. There was little to no correlation between tubulointerstitial disease and

graft failure, DGF, or eGFR. While Hall et al demonstrated that the risk of DGF was increased in kidneys with acute tubular necrosis ($_{1.23}1.59_{2.06}$), this finding was limited to kidneys from donors after circulatory death and did not appear associated with decrements in long-term outcome.[19,20]

To address the limitations inherent in procurement biopsy results, multiple scoring systems have been developed, which combine various pathological findings (with or without additional donor factors) to assess the likelihood of early graft failure.[11] In their systemic review, Wang et al reported that only half of the fifteen studies examined demonstrated an association between biopsy scores and graft failure rates and graft function. In 2004, Howie et al reported retrospectively assessed donor morphology for 500 allografts and developed an index of chronic injury.[21] The index was strongly correlated with donor age, and, after adjustment for age, only an index of 40% or greater (<2% of all kidneys) was associated with worse outcome. The Maryland Aggregate Pathology Index (MAPI) was published in 2014 using contemporary analysis of wedge biopsies.[22] The score combines GS, arterial-wall-to-lumen ratio, scar/fibrosis in at least 10 tubules, and arteriolar hyalinosis. Increasing scores were associated with similar 1-year but reduced 3-year survival (low MAPI, 84.3%; intermediate MAPI, 56.5%; high MAPI, 50%; *P* <0.0001), a finding that was replicated at a second unaffiliated center. However, only 5% of allografts had a high MAPI score. The impact of MAPI score was found to be independent of age, ECD classification, and high terminal creatinine. To support the value of procurement biopsy in high-risk kidneys, the authors point out that up to 20% of high-KDPI kidneys have a low MAPI score and would be expected to produce good outcomes.

Logistical and technical factors appear to contribute to the poor reliability of kidney allograft biopsy results. Deceased donor recovery often occurs at remote hospitals during off hours, and frozen section interpretation may be performed by pathologists without subspecialty training in renal pathology. However, interrater reliability is limited even among experts. In their seminal publication on the Banff Histopathological Consensus Criteria for Pre-implantation Kidney Biopsies, Liapis et al reported the interrater reliability for a sample of 19 pre-implantation biopsies (frozen and permanent) reviewed by 32 trained pathologists.[10] In frozen section core biopsies, the interclass correlation coefficient (ICC) was less than 0.4 for all characteristics including GS (>0.75 is considered good). The ICC for interstitial fibrosis, arteriolar hyalinosis, and tubular injury were all less than 0.1. In the wedge frozen section, only the ICC for GS was greater than 0.6, and scores for interstitial fibrosis, inflammation, arterial hyalinosis, and tubular injury were all fair to poor (ICC <0.5). Given that these biopsies were reviewed by trained pathologists without time pressure, real-world reliability is highly likely to be similar or worse. In addition, obtaining a biopsy appears to increase cold ischemia times for transplanted organs. Because longer cold ischemia times have well-established associations with higher rates of delayed graft

function, in addition to affecting the likelihood of discard, obtaining an *un*necessary biopsy may potentially harm outcomes for organs that are used for transplant.

Among the limitations of all biopsy studies is the inherent bias resulting from discarding organs with biopsy results that were believed to be associated with poor outcomes. The outcome of these grafts is, generally, unknown, and therefore the predictive power of the scoring systems in identifying at-risk organs may actually be greater. Unique among these reports is that by De Vusser, outlining the Leuven index, which was described for 548 transplant recipients with renal biopsy specimens that were not used to determine transplant suitability, and were divided into a development and validation cohort.[23] Using logistic regression analysis, the authors combined pathologic score for interstitial fibrosis/tubular atrophy according to the Banff'07 classification, percentage GS, and donor age. A Leuven score >47 had an 85% specificity and 81% sensitivity for graft failure within 5 years. The authors further validated the score comparing frozen sections, demonstrating that the results were highly correlated (r = 0.99, *P* <0.0001). Despite the apparent predictive value of the Leuven score, its utility in identifying allografts that should be discarded is limited. Hall et al described a prospective study examining Leuven score, KDPI, organ discard, and graft failure in a US population of donors.[19] Kidney biopsy was performed according to standard practice and varied from 16% to 87% across the five OPOs in the study. Leuven score and KDPI were tightly correlated (rho = 0.726, *P* <0.0001). Among 1,729 organs selected for biopsy, 34% were eventually discarded. There was no difference between KDPI and Leuven score in the area under the curve (AUC) (0.72) for predicting discard, although the correlation between discard and score was stronger for Leuven score. Among transplanted kidneys, the AUCs for models predicting graft failure were modest and similar (0.62 and 0.61), suggesting that neither score provides a highly accurate assessment of graft function. In models including both scores, the Leuven score was no longer statistically significant after adjusting for KDPI. Neither scoring system accurately predicted DGF (AUC 0.5 and 0.53). The authors conclude that neither KDPI nor Leuven score is sufficiently accurate to dictate organ discard, particularly in light of data suggesting that even very "marginal" kidneys provide significant benefit for appropriately selected candidates.[5] However, it is not possible to know how the organs that were discarded "for cause" would have performed in this analysis if they had been transplanted.

Data from the current study address, in part, the ongoing issue of confounding by indication for biopsy. Nationally, we demonstrate that kidneys with largely similar clinical and laboratory indications are biopsied at different rates on the basis of OPO and center practice. These data confirm that the decision to biopsy significantly increases the risk-adjusted rate of discard for all organs with KDPI <85.

Importantly, for organs with a KDPI >85, we found less variation in biopsy rates and aORs for discard related to biopsy (aOR, $_{0.9}1.2_{1.5}$).

The demonstration of variation in biopsy rates due to underlying clinical differences has led to efforts by the transplant community to standardize biopsy use and reduce use for low-risk kidneys, as the biopsy does not appear to add substantially to clinical information. For high-KDPI organs, the transplant community should consider options to increase the reliability of biopsy findings. These strategies include use of wedge biopsies for frozen section (based on the Banff recommendations), telepathology solutions to provide whole-slide imaging to a core group of trained pathologists who can provide real-time morphometric analysis, and allocation of kidneys with higher-risk biopsy findings to appropriately selected patients in transplant programs willing to use them, potentially in the context of dual organ transplant.

This study has important limitations. First, these data are retrospective and it is likely that some lower-risk kidneys underwent biopsy for specific clinical indications not included in the KDPI (e.g., acute kidney injury), which would be expected to increase discard. However, the marked variation in biopsy use in this population across OPOs suggests that OPO and program preferences rather than clinical indications largely drive these decisions. Notably, whether to biopsy organs is a joint decision of the OPO and the transplant program, and there is no clear way to discriminate decisions at the transplant program level with the available data. Second, we studied only the decision to biopsy; the detailed pathologic findings obtained as a result were not examined in this study. However, given low ICCs and poor correlation of biopsy findings and outcomes, it is not clear that these data would substantially improve the precision of this analysis. Third, our study was performed just after implementation of the revised kidney allocation system, which included provisions intended to improve use of high-risk organs. However, as noted, the impact of biopsy on discard rates did not decrease over time, suggesting that the change in allocation system did not diminish the significance of the effects described here. Finally, we did not examine organ outcomes by biopsy status in the current study, and therefore determination of the percentages of organs discarded appropriately requires ongoing investigation.

In conclusion, despite 20 years of data demonstrating that biopsies performed at the time of kidney recovery provide limited insight regarding the eventual outcome of renal allografts, more than 50% of organs are still biopsied. This decision is highly associated with kidney discard rates, and may not significantly enhance information on outcomes beyond that available using clinical criteria (e.g., age, KDPI). As per a recent report from a National Kidney Foundation consensus conference, efforts to decrease kidney discards may be strengthened by developing standards for biopsy use that could be informed by a randomized trial to help define the benefits and harms of procurement biopsies.[24] Pursuit

of evidence to guide appropriate biopsy use, along with development of strategies to improve the quality of kidneys at higher risk for discard (intervention research), motivate acceptance, and expedite placement, are vital priorities to reduce unnecessary discard and increase access to transplant for patients in need.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation.*

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FIGURE LEGENDS

Figure 1. National US deceased donor kidney biopsy and discard rates across OPOs (December 2014-August 2018), (A) overall and at (B) KDPI <20 and (C) >85. Each bar represents one of the 58 US OPOs. KDPI-stratified displays are sorted in the same order. National average unadjusted biopsy rate with KDPI <20 and >85: 17.0% and 95.5%; respectively. National average unadjusted discard rate with KDPI <20 and >85: 3.5% and 64.7%; respectively. KDPI, kidney donor profile index; OPO, organ procurement organization.

Figure 2. Unadjusted national kidney discard rates, by biopsy status and KDPI strata. KDPI, kidney donor profile index.

Figure 3. Relationships of cold ischemia times with biopsy and discard rates across OPOs.

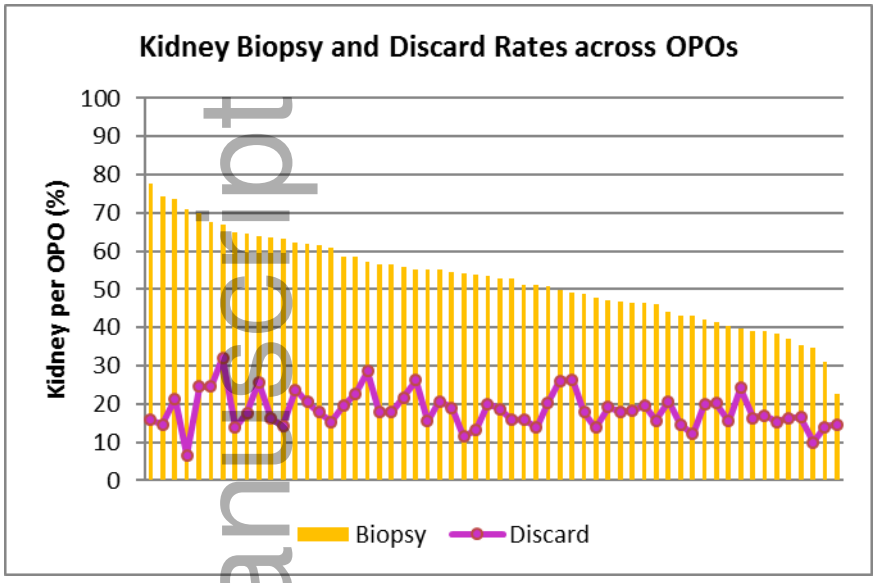
Figure 4. Adjusted relationships of biopsy with discard, across KDPI strata. KDPI, kidney donor profile index

Figure 5. Empirical Bayes estimates for likelihood of kidney biopsy across OPOs by KDPI strata. KDPI-stratified models and include adjustment for additional donor factors in the registry. The red bar demonstrates the national average rate of biopsy, adjusted for donor factors in the model. Each red dot represents adjusted biopsy rate at one OPO, and the blue bars reflect 95% CIs for use at the OPO determined by empirical Bayes estimates adjusting for OPO and donor factors; exclusion of the national average by a 95% CI reflects adjusted biopsy rates significantly above or below the national average. The reference donor is defined by the absence of the included donor factors (i.e., hepatitis B core antibody negative, cytomegalovirus negative, Epstein Barr virus negative, no substance use). CI, confidence interval; KDPI, kidney donor profile index; MOR, median odds ratio; OPO, organ procurement organization.

Figure 6. Empirical Bayes estimates for discard rates across OPOs by KDPI strata and biopsy performance status: (A) with biopsy; (B) without biopsy. KDPI-stratified models and include adjustment for additional donor factors in the registry. The red bar demonstrates the national average rate of biopsy adjusted for donor factors in the model. Each red dot represents adjusted discard rate at one OPO, and the blue bars reflect 95% CIs for use at the OPO determined by empirical Bayes estimates adjusting for KDPI and OPO; exclusion of the national average by a 95% CI reflects adjusted discards rates use significantly above or below the national average. The reference donor is defined by the absence of the included donor factors (i.e., hepatitis B core antibody negative, cytomegalovirus negative, Epstein Barr virus negative, no substance use). CI, confidence interval; KDPI, kidney donor profile index; MOR, median odds ratio; OPO, organ procurement organization.

Figure 1.

A.



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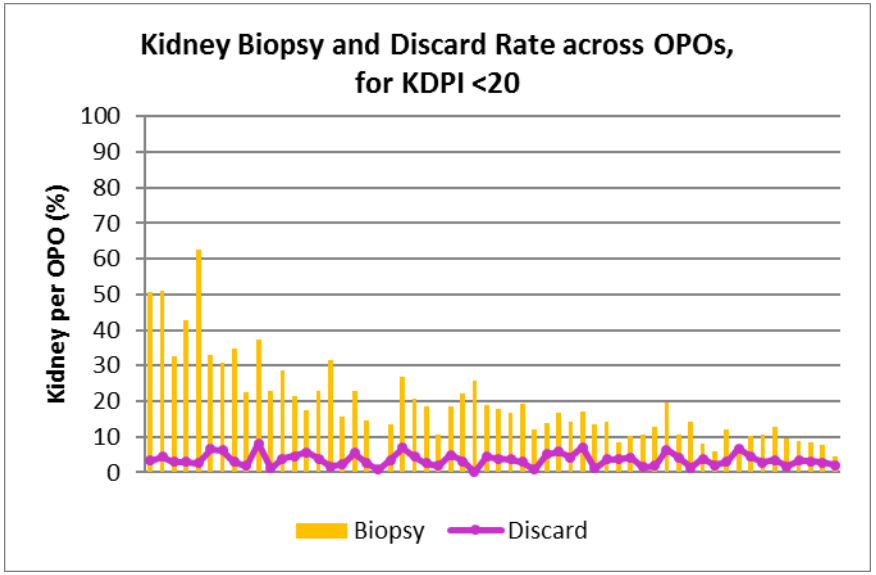

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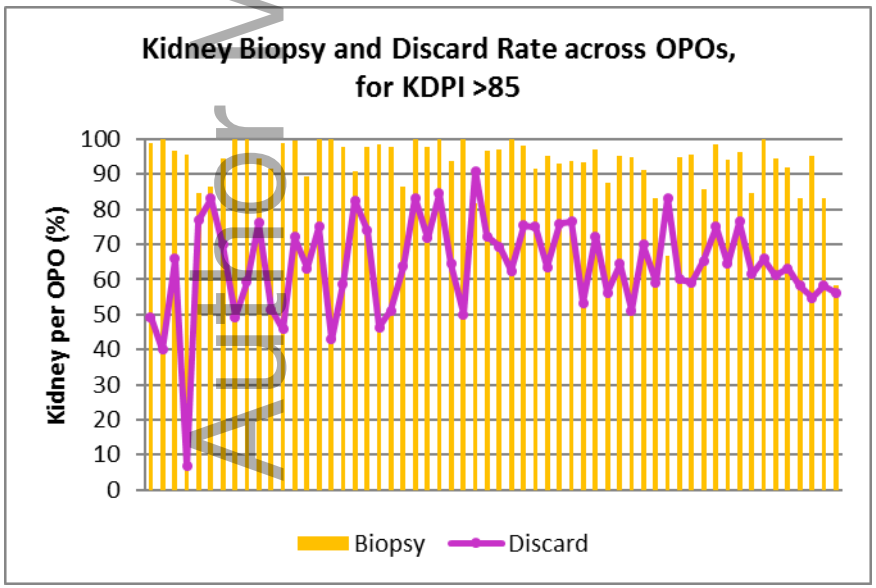

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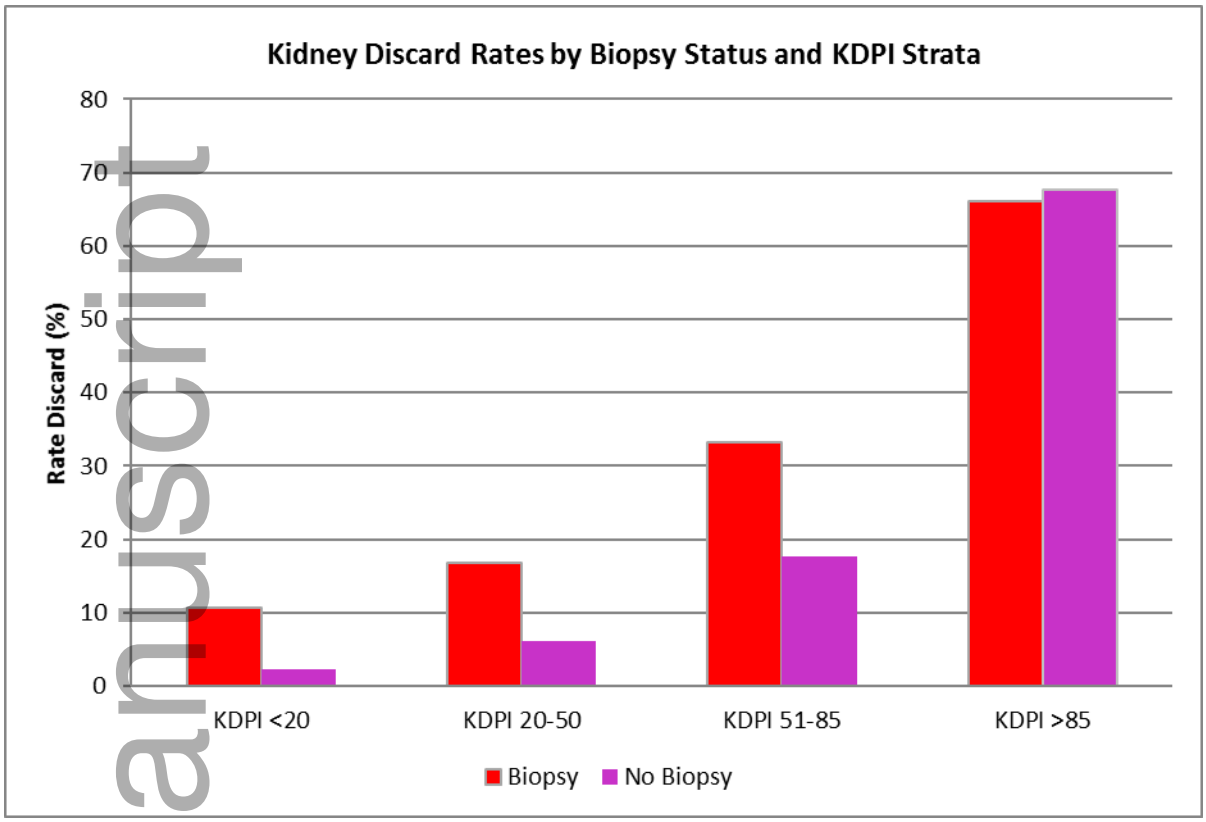
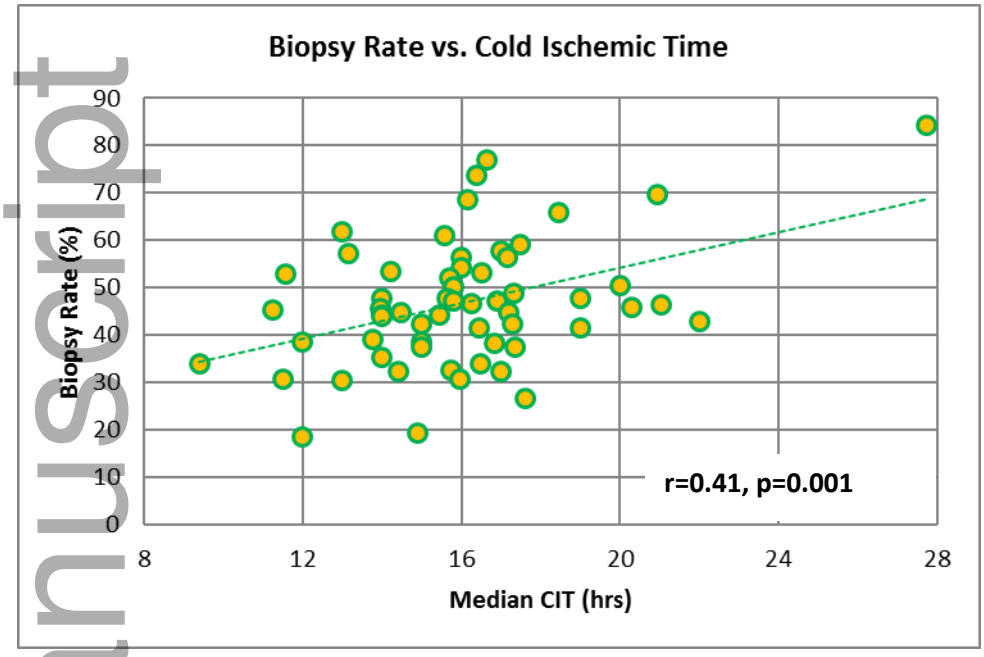


Figure 3.

A.



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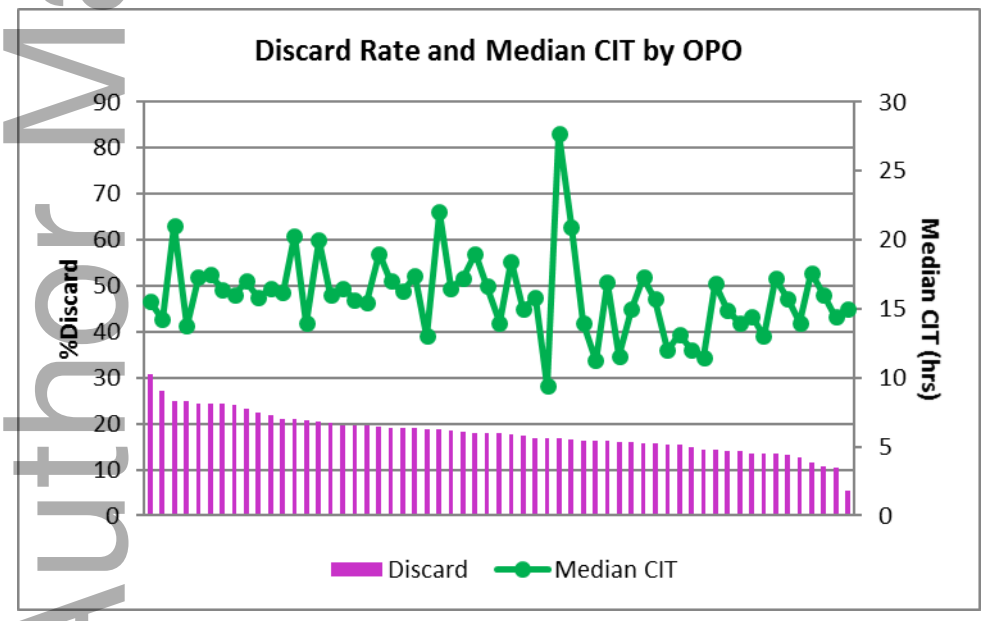
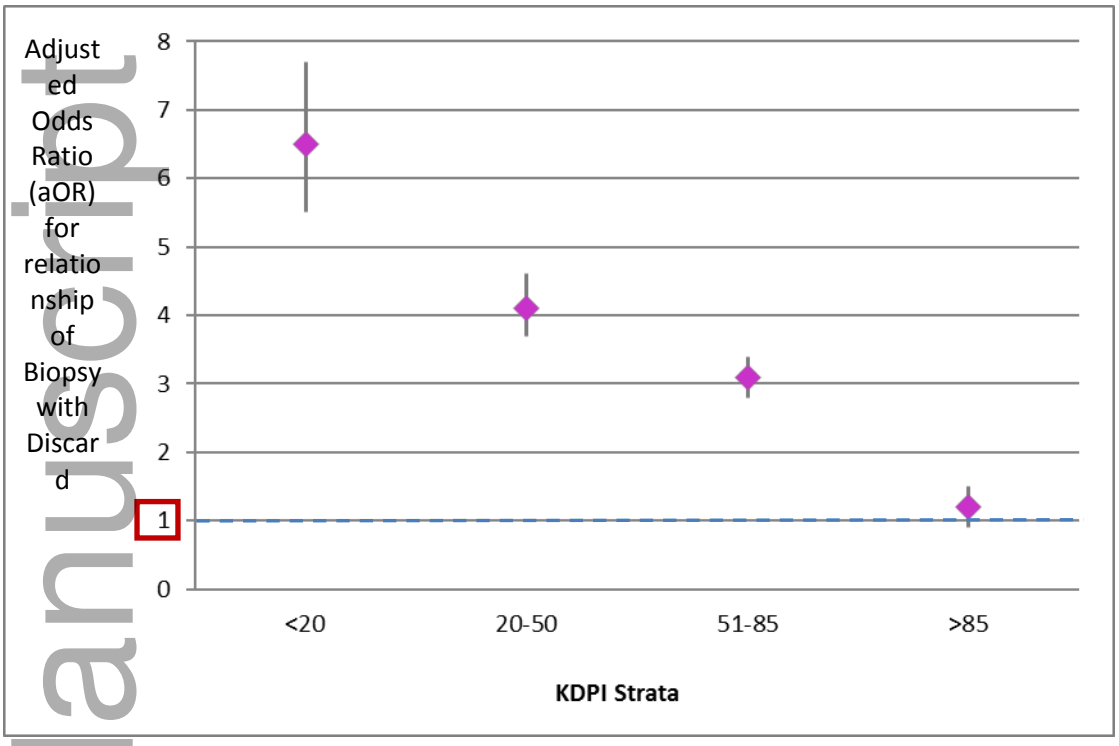


Figure 4.



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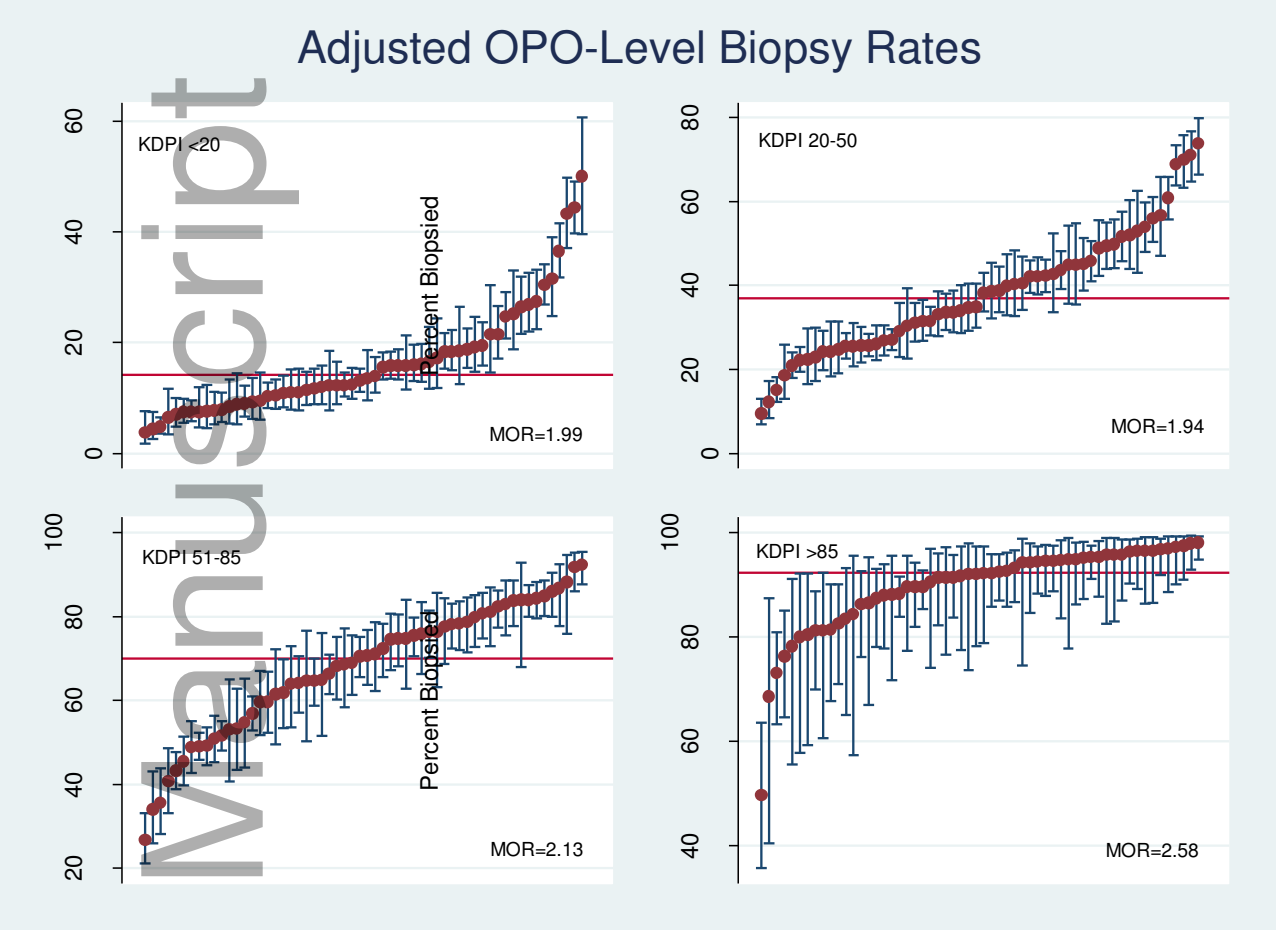
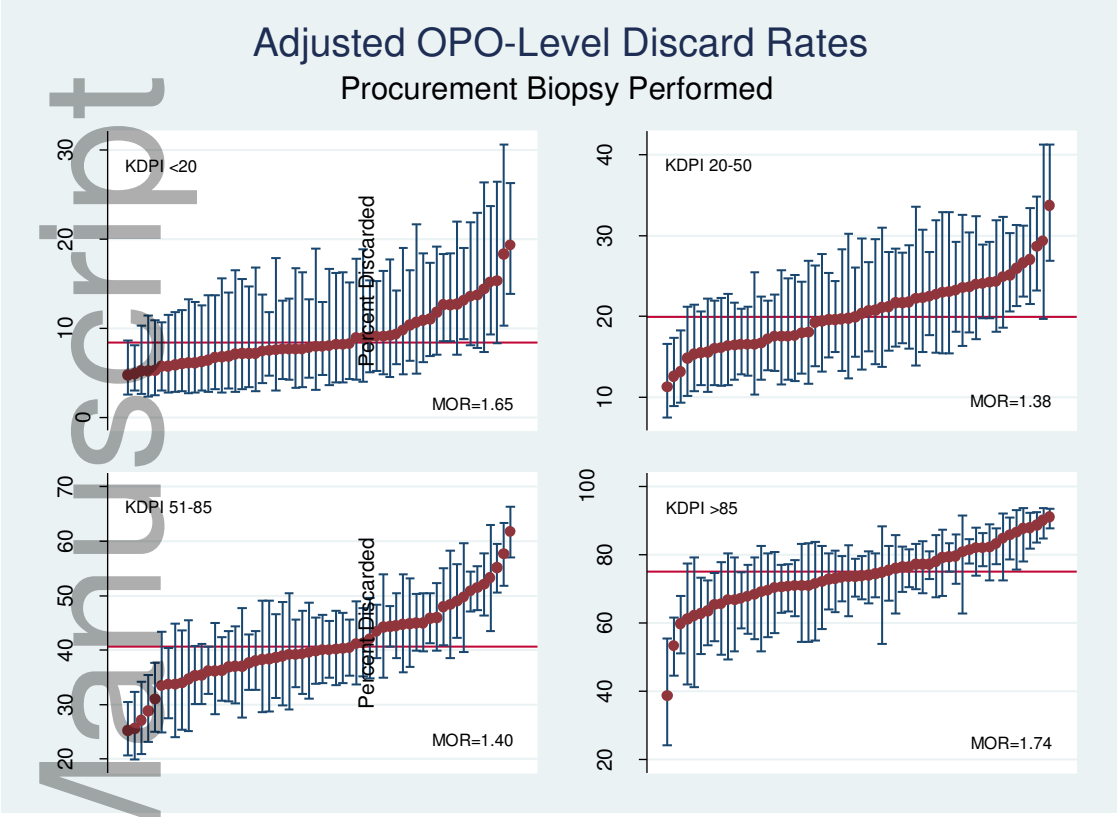


Figure 6.

A.



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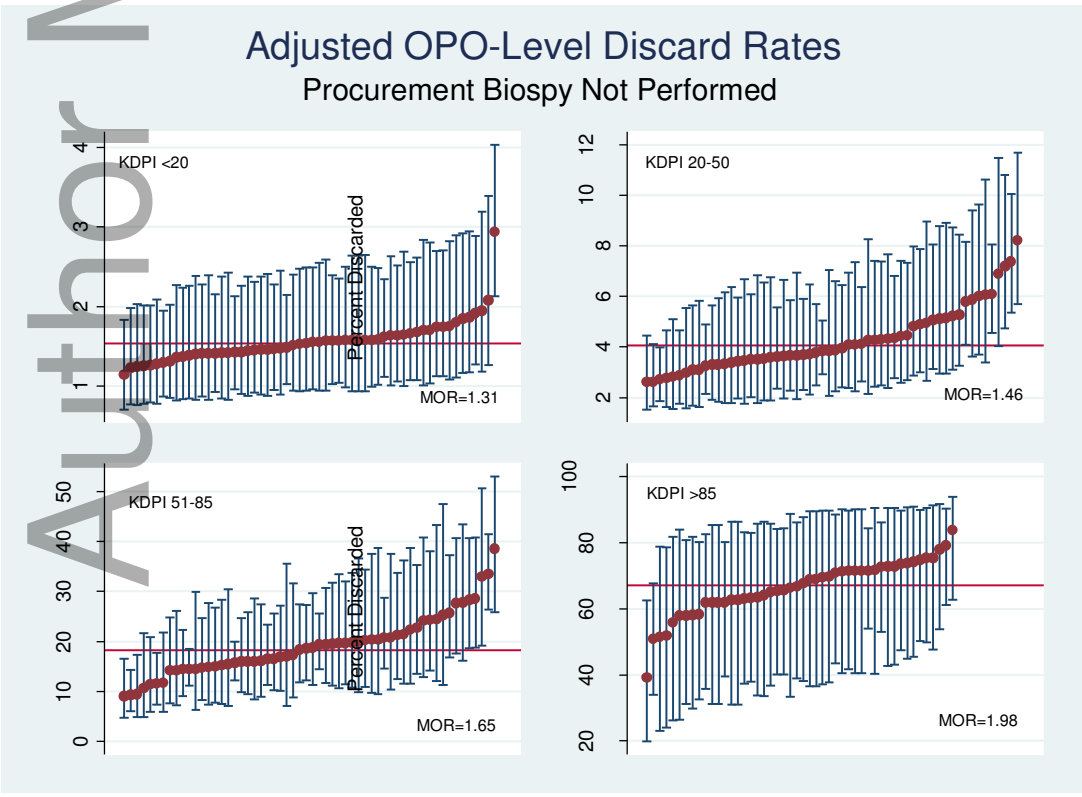

Table 1. Unadjusted frequencies of biopsies and discards among deceased donor kidneys procured for transplant in the US, 2014-2018 (*n* = 59,328)

	Kidneys in Each Factor Level (*n* = 59,328)	**Biopsy % (*n* = 31,272)**	**Discard % (*n* = 11,538)**
KDPI levels, %		ǂ	ǂ
<20	18543	18.7	3.8
20-50	18353	49.0	11.4
51-60	5442	72.5	21.3
61-70	4829	80.0	27.2
71-85	6669	87.2	39.6
>85	5492	94.5	66.2
Other donor factors			
Hepatitis B core antibody positive	2427	73.1ǂ	34.9ǂ
CMV positive	36074	54.6ǂ	20.9ǂ
EBV IgG positive	53037	53.8ǂ	19.9ǂ
Cancer	2003	73.8ǂ	35.7ǂ
Smoking	11920	73.7ǂ	30.8ǂ
Alcohol use	11215	62.1ǂ	20.1
Cocaine use	5621	48.6ǂ	15.8ǂ
Other drug use	26392	47.1ǂ	15.8ǂ
Vasodilators use	7201	53.1	19.3
PHS with HCV seropositive	2614	47.4ǂ	37.8ǂ
PHS without HCV seropositive	11320	46.2ǂ	13.2ǂ
Pump kidney	20150	66.8ǂ	15.4ǂ

Percentages reflect the proportions of kidneys from donors with a given clinical trait (e.g., specified KDPI level) that were biopsied and discarded, respectively (i.e., row percentages). Donor factors included in the computation of KDPI include: age, height, weight, race, history of hypertension, history of diabetes, cause of death, serum creatinine, HCV status, and donation after circulatory death. CMV, cytomegalovirus; EBV, Epstein Barr virus; HCV, hepatitis C virus; KDPI, kidney donor profile index; PHS, Public Health Service.

Table 2. Associations of KDPI and other donor factors with likelihood of kidney biopsy and discard in a multi-level model also adjusted for OPO

Donor Characteristics	**Biopsy aOR (95% CI)**	**Discard aOR (95% CI)**
Biopsy performed	N/A	3.51 (3.29-3.76)‡
KDPI levels, %		
<20	0.22 (0.21-0.23)‡	0.48 (0.44-0.53)‡
20-50	Reference	Reference
51-60	2.90 (2.70-3.11)‡	1.73 (1.59-1.88)‡
61-70	4.52 (4.17-4.89)‡	2.32 (2.13-2.52)‡
71-85	8.15 (7.51-8.85)‡	3.96 (3.68-4.26)‡
>85	21.36 (18.88-24.16)‡	11.18 (10.31-12.12)‡
Other donor factors		
Hepatitis B core antibody positive	1.18 (1.06-1.32)*	1.04 (0.94-1.15)
CMV positive	0.97 (0.93-1.02)	1.04 (0.99-1.09)
EBV IgG positive	1.42 (1.31-1.54)‡	0.92 (0.83-1.02)
Cancer	1.18 (1.04-1.33)*	1.16 (1.04-1.30)*
Smoking	1.65 (1.57-1.75)‡	1.34 (1.27-1.42)‡
Alcohol use	1.33 (1.26-1.40)‡	0.89 (0.83-0.94)‡
Cocaine use	0.96 (0.90-1.04)	0.76 (0.70-0.84)‡
Other drug use	1.06 (1.02-1.11)*	0.95 (0.90-1.01)
Vasodilators use	0.89 (0.83-0.96)†	0.96 (0.88-1.04)
PHS with HCV seropositive	0.61 (0.55-0.67)‡	4.53 (4.08-5.03)‡
PHS without HCV seropositive	1.19 (1.12-1.25)‡	1.14 (1.06-1.22)†
Pump Kidney	N/A	0.47 (0.44-0.50)‡

P-values: * p<0.05 –0.002; † p=0.001 –0.0002; ‡ p<0.0001

The reference KDPI level is 20%-50%. The representative donor is defined by the absence of all the donor factors identified in the registry (i.e., hepatitis B core antibody negative, CMV negative, EBV negative, no substance use). CMV, cytomegalovirus; EBV, Epstein Barr virus; HCV, hepatitis C virus; KDPI, kidney donor profile index; OPO, organ procurement organization; PHS, Public Health Service.

Table 3. OPO level measures of heterogeneity in biopsy and discard practices, with and without adjustment for donor factors

	Biopsy	Discard
MOR, null model	1.57	1.34
MOR adjusted for KDPI	1.91	1.35
MOR adjusted for KDPI + other donor factors	1.94	1.34
MOR adjusted for KDPI + other donor factors + performance of biopsy	NA	1.36
No. of OPOs significantly above reference probability before adjustment (null model)	21	15
No. of OPOs significantly above reference probability after adjustment	24	18
No. of OPOs significantly below reference probability before adjustment (null model)	23	14
No. of OPOs significantly below reference probability after adjustment	23	11

Models are adjusted for KDPI and other donor factors in the registry. For discard, the models also include biopsy performance. KDPI, kidney donor profile index; MOR, median odds ratio; OPO, organ procurement organization.

Table 4. Adjusted variation in OPO discard rate by KDPI levels, A) among biopsied kidneys and B) among kidneys that were not biopsied

A. Biopsied

	No. of OPOs significantly above reference probability	No. of OPOs significantly below reference probability	Population averaged predicted discard rate	MOR
KDPI Levels, %				
<20	6	1	8.4	1.65
20-50	6	3	19.9	1.38
51-85	10	7	40.7	1.40
>85	10	7	75.2	1.74

B. Not biopsied

	No. of OPOs significantly above reference probability	No. of OPOs significantly below reference probability	Population averaged predicted discard Rate	MOR
KDPI Levels, %				
<20	1	0	1.5	1.31
20-50	5	1	4.1	1.46
51-85	5	4	18.2	1.65
>85	10	1	67.2	1.98

KDPI, kidney donor profile index; MOR, median odds ratio; OPO, organ procurement organization.