Renal Function at Discharge Among Kidney Recipients Experiencing Delayed Graft Function and Its Associations With Long-term Outcomes

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Background. Delayed graft function (DGF) after kidney transplantation is associated with higher rates of acute rejection and poor graft survival and outcomes. Current DGF definitions based on posttransplant need for dialysis are not standardized and there are no objective methodologies for quantifying DGF severity. Methods. Using Organ Procurement and Transplantation Network data, we examined DGF, and used recipient serum creatinine at discharge as a correlate of renal function and DGF severity (mild: <2.5 mg/dL; severe: ≥2.5 mg/dL). The associations between donor and recipient factors and DGF severity were quantified using logistic regression. We also examined the associations between DGF severity and long-term recipient outcomes, adjusting for potential confounders. Results. A predictive model using donor and recipient factors had a reasonably good ability to discriminate mild (low creatinine) versus severe (high creatinine) DGF (c-statistic of 0.70). In Cox regression, DGF and creatinine at discharge were both independently associated with long-term outcomes, yet their effects differed depending on the outcome (graft function, death-censored graft function, recipient mortality). Our findings suggest that having DGF, but with relatively good renal function (creatinine <2.5) at discharge, may be less deleterious on graft and recipient survival compared with severe, prolonged DGF, which was associated with a decreased median graft survival of ~2.6 y compared with no DGF with low creatinine at discharge. Conclusions. Our novel DGF severity stratification identified unique factors associated with DGF severity, along with DGF’s association with long-term graft and patient survival. The adverse cost and outcome implications of severe DGF warrant additional investigation to improve kidney transplantation practice.

(Diagram of the process)

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Delayed graft function (DGF), a common early complication after kidney transplantation (KT), is often defined as “the need for dialysis in the first week after KT.” DGF occurrence ranges from 4–50% in KT patients, depending on the definition used, with a conservative estimate of ~31% for recipients of deceased donor kidneys in US transplant centers.1 Because DGF is a form of early posttransplant acute kidney injury and typically necessitates dialysis, it is associated with higher rates of acute rejection, thereby impacting graft survival.2,3 DGF patients have a 41% increased risk of graft loss when compared with patients without DGF at ~3 y posttransplant.4 DGF has also been associated with higher medical costs, and this may be influenced by the definition of DGF used.5–7 The Food and Drug Administration has recognized DGF as a clinically relevant endpoint for drug development based on clinical trials of drugs demonstrating early improvements in DGF, although none have demonstrated late graft function improvement.8 DGF is also higher in donors with circulatory determination of death (DCD) compared with standard criteria donors but with comparable long-term outcomes.9,10 Disparities in DGF rates can be attributed mostly to the lack of a standard definition for DGF. Although the need for dialysis immediately posttransplant is the most documented definition, its major limitation is that indications for
dialysis are not standardized and vary depending on the clinician and transplant center. Therefore, a superior, consistent, and objective definition is needed to quantify early graft dysfunction and its short- and long-term effects. The common definitions in use, mostly defined by single-center studies, have been repeatedly challenged. A study analyzing 22 different definitions of DGF based on dialysis, serum creatinine or urine output showed a disparity in DGF incidence depending on the definition. Perhaps the most important limitation is the lack of an objective methodology for quantifying graft dysfunction and its severity during and after a DGF episode. Delineating DGF severity may afford better estimations of subsequent outcomes in patients and may help identify avenues for altering and even prolonging graft and patient survival and decrease the reluctance of clinicians’ acceptance of kidneys at higher risk of DGF.

Previous studies have attempted to classify DGF severity as mild or severe, based on serum creatinine reduction ratio from posttransplant day 1 to day 2 (creatinine reduction 2) plus 24-h urine creatinine excretion (urine creatinine 2). A model to predict DGF based on several donor and recipient characteristics at time of transplantation had a c-index that was moderately predictive (0.71), and included more donor and recipient characteristics than a previous model published by the same group with a c-index of 0.665. Another model that simplified the number of predictors based on easily available demographic and clinical features demonstrated an area under the receiver operating characteristic curve of 0.63 with potential to be used in routine clinical practice without the need for extensive amounts of data.

MATERIALS AND METHODS

OPTN data on all donors, wait-listed candidates, and transplant recipients in the United States were used. Trend analysis included single KTs performed from January 1, 2000, to December 31, 2017, and included both deceased and living donor transplants. Subsequent analyses included only deceased donor transplants. To determine donor/recipient factors associated with mild versus severe DGF based on creatinine at discharge in the Kidney Allocation System (KAS) era (phase II), our cohort consisted of single, adult, deceased donor KT recipients from 2015 to 2018. Recipients with a graft failing before discharge or having length of stay (LOS) >21 d were excluded, as we assumed such cases reflect severe complications outside the scope of our study of mild and even severe DGF. Preemptively transplanted recipients (those not yet on dialysis before transplant) were included because they are not immune to experiencing DGF. Among recipients dia- lyzed within a week of transplant (ie, having DGF according to the standard definition), logistic regression modeling was performed to identify factors associated with having mild (discharge serum creatinine <2.5 mg/dL) or severe (≥2.5) DGF. Because the OPTN registry does not indicate which recipients were still on dialysis at the time of discharge, we avoided using estimated glomerular filtration rate (eGFR) as a proxy for DGF severity because Modification of Diet in Renal Disease and Chronic Kidney Disease Epidemiology Collaboration formulae were not developed or validated on patients receiving dialysis.

To produce interpretable, clinical prediction models and reliable statistical inference, we followed the general modeling approach of Harrell. Predictor variables were included based on a priori clinical hypothesis generation using subject matter expertise and existing literature. LOS was included as a covariate to adjust for its association with posttransplant serum creatinine trajectory and differential center practices regarding timing of discharge. To avoid overfitting, the number of model parameters was limited to allow far >15 events per degree of freedom. Restricted cubic splines were used to parameterize continuous variables expected to have substantial and possibly nonlinear effects. Multiple imputation was used to handle the 11% of records with at least 1 missing covariate. Model performance was measured using the c-statistic and calibration plots and bootstrapping was performed to produce bias-corrected assessments of both model discrimination and calibration. In a sensitivity analysis, we modeled serum creatinine at discharge among DGF recipients as a continuous variable to complement the binary outcome analysis.

We numerically and graphically assessed the correlation between our DGF severity prediction model and Irish’s DGF prediction model on nonpumped KTs from 2015 to 2018 to highlight the degree to which these models are nonredundant and to generate novel insights from the new model. LOS was held constant at 5 d when exercising the DGF severity model. For the Irish model, calculated panel reactive antibody replaced “peak Panel-Reactive Antibody” and recipients were assumed to have no blood transfusions because this measure is no longer collected.

Finally, we used an older (2008–2015), at-discharge cohort with the same exclusions to evaluate the associations between DGF and creatinine at discharge and long-term kidney graft survival, death-censored graft survival, and recipient survival (phase III). We conducted Kaplan-Meier analysis and Cox regression, adjusting for various covariates to isolate the effects of the primary exposures of interest (DGF, creatinine at discharge). Multiple imputation was used to accommodate the 7% of records with a missing covariate. All analyses were
RESULTS

Background Data

Among single kidney deceased donor transplants from 2000 to 2017, DGF was markedly higher in deceased donor recipients versus living donors (25.2% versus 3.9%; \( P < 0.00001 \); Figure 1). There was a significant difference in DGF between adults and pediatric recipients of kidneys (17.8% versus 7.2%; \( P = 0.00001 \)). Similarly, DGF was also higher in males versus female recipients (19.0% versus 14.7%; \( P = 0.00001 \)).

Phase I

The distribution of serum creatinine before transplant for dialysis versus preemptive KT patients is shown in Figure S1 (SDC, http://links.lww.com/TXD/A476). In fact, 8% of preemptive recipients from 2015 to 2018 experienced DGF. Though our use of creatinine to assess renal function among recipients who may be receiving dialysis is imperfect, the top panel shows that the administration of dialysis virtually never results in creatinine values so misleadingly low (<2.5 mg/dL) as to suggest “good” renal function in a population of patients who, being listed as a transplant patient, by definition have poor renal function. Table 1 shows that 90.6% of the patients who experienced DGF were determined to have “severe DGF” (Cr ≥2.5 mg/dL) and only 9.4% have “mild DGF” (Cr <2.5 mg/dL).

Phase II

A total of 12,856 DGF recipients were included in modeling the probability of a high versus low creatinine at discharge (proxy for DGF severity; Table 1). The degree to which various donor and recipient risk factors are associated with differential degrees of DGF is shown via a forest plot (Figure 2). Among DGF recipients, greater height (178 versus 162 cm) was strongly associated with severe versus mild DGF (odds ratio [OR], 1.63; 95% confidence interval [CI], 1.32-2.02), followed by body mass index (BMI; 32 versus 24.1; OR, 1.49; 95% CI, 1.25-1.78), and time on dialysis (6.6 versus 1.9 y; OR, 1.24; 95% CI, 1.08-1.42, 1.42). Significant donor factors included being a DCD donor (OR, 4.94; 95% CI, 2.10-11.62), age (50 versus 26 y; OR, 1.65; 95% CI, 1.36-2.01), cold ischemic time (22.8 versus 11.6 h; OR, 1.43; 95% CI, 1.22-1.67), height (179 versus 165 cm; OR, 0.8; 95% CI, 0.71-0.90), terminal eGFR (117 versus 59 mL/min; OR, 0.76; 95% CI, 0.63-0.92), and female sex (OR, 0.72; 95% CI, 0.58-0.90). We note that the apparent relationship between recipient female sex and lower odds of a high creatinine at discharge may merely reflect inherent, sex-based differences in creatinine production, as opposed to severe versus mild DGF; in fact, in a preliminary analysis (not shown) modeling eGFR at discharge instead of creatinine, the effect of sex was almost entirely attenuated. The risk-adjusted relationships between several highly predictive continuous variables and
the likelihood of severe DGF are shown in Figure 3. Recipient BMI was the most predictive factor for severe DGF, with low BMI having a strong protective effect ($P < 0.001$; Figure 3A). Shorter recipients (height <150 in) had significantly better odds of low creatinine at discharge (Figure 3B). Recipients on dialysis for >5 y were at increased risk of severe DGF (Figure 3C). Among donor variables, terminal eGFR was highly predictive, and low terminal eGFR was associated with severe DGF. Elevated pumping resistance was associated with higher odds of severe DGF, although this relationship was only of borderline statistical significance ($P = 0.09$). Older and shorter donors were also predictive of severe DGF (Figures 4A–D), respectively. The logistic regression model of donor and recipient variables had reasonably good ability to discriminate high versus low creatinine at discharge among DGF cases, with a bias-corrected c-statistic of 0.70.

### TABLE 1

| Creatinine at discharge | DGF | Non-DGF |
|-------------------------|-----|---------|
|                        | N   | %       | N   | %       |
| <1                     | 72  | 0.6     | 2494| 7.6     |
| 1–1.25                 | 139 | 1.1     | 3202| 9.7     |
| 1.25–1.5               | 145 | 1.1     | 2948| 9.0     |
| 1.5–2                  | 411 | 3.2     | 5273| 16.0    |
| 2–2.5                  | 431 | 3.4     | 3665| 11.1    |
| 2.5–3                  | 465 | 3.6     | 2664| 8.1     |
| 3–4                    | 1173| 9.1     | 3735| 11.4    |
| ≥4                     | 10200| 77.9   | 8921| 27.1    |
| Total                  | 12856| 100    | 32902| 100    |

DGF, delayed graft function.

**FIGURE 2.** Donor and recipient risk factors associated with differential degrees of DGF. BMI, body mass index; CPRA, calculated panel reactive antibody; DCD, donors with circulatory determination of death; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; HCV, hepatitis C virus; IL-2, interleukin 2; MMF, mycophenolate mofetil; NAT, nucleic acid testing; OPO, organ procurement organization; TAC, tacrolimus; TX, transplant; TXC, transplant center.
We used the model to predict the probability of a KT recipient with DGF having a creatinine of ≥2.5 at discharge for 5 recipient profiles of varying BMI, height, cold ischemia time, donor age, donor eGFR, and Organ Procurement Organization decision to pump the kidney (Table 2). Predicted probabilities of severe DGF varied markedly, ranging from 48% to 99%.

Although our DGF severity model predictions were highly correlated \( r = 0.71, P < 0.0001 \) with DGF predictions from the Irish model, significant scatter about the \( y = x \) identity line suggests for many patients that the model predictions are somewhat discordant (Figure 5A). Examining 2 groups of recipients (A and B) both having Irish probability of DGF predictions in the 3% to 6% range yet with very different probabilities of severe DGF (conditional on having DGF) aids in pinpointing differential clinical insights afforded by our new model (Figure 5B). Compared with group B recipients \( (n = 58) \), group A recipients \( (n = 24) \) had much lower creatinine before transplant (median: 4.1 versus 9.6 mg/dL) and were shorter in stature (median: 157.4 versus 177.8 cm), reflecting 2 covariates found to be highly predictive in our model but absent from the Irish model. Furthermore, no group A recipients experienced severe DGF compared with 29% of group B recipients \( (P = 0.002) \).

When serum creatinine at discharge was modeled as a continuous response variable, the factors found to be highly associated with differences in renal function at discharge were generally like those found in the binary (logistic) response modeling, except for race/ethnicity being significantly different. Like the primary analysis, Figure S2 (SDC, http://links.lww.com/TXD/A476) shows that recipient height, recipient BMI, donor DCD status, and whether the kidney was pumped were all factors associated with differential degrees of kidney function (creatinine at discharge) among recipients receiving dialysis within the first week after transplant.

**Phase III**

We next aimed to characterize how differing degrees of DGF severity are associated with long-term recipient and graft outcomes, and specifically whether DGF was associated with outcomes independently of recipient creatinine at discharge. This was done on an independent at-discharge cohort with the same exclusions as phase II (2008–2015), to evaluate kidney graft survival, death-censored graft survival, and recipient survival. In this cohort, median follow-up times exceeded 5 y for each of the 3 outcomes, and the number of events was large (graft failures: 22,778; death-censored failures: 11,489;
When we compared DGF and creatinine in recipients experiencing DGF to those without DGF, the results showed that DGF and creatinine were highly correlated at the time of discharge. Only 9.6% of patients with DGF had a discharge creatinine of <2.5, compared with 53.4% of non-DGF patients (Table 1). By contrast, 77.9% of DGF recipients had discharge creatinine of ≥4, compared with just 27.1% of patients who did not experience DGF.

The Cox regression models had c-statistics of 0.65, 0.68, and 0.71 for all-cause graft failure, death-censored graft failure, and patient mortality, respectively. Compared with recipients not experiencing DGF and having creatinine of <2.5 at discharge, all other groups had statistically higher risks of long-term all-cause graft failure ($P<0.001$) in both unadjusted and adjusted analyses (Table 3). Most notably, recipients experiencing DGF and having high creatinine (≥2.5) at discharge had a 49% higher risk-adjusted hazard of graft failure compared with the reference group. The elevated graft failure hazard for these patients was even higher (hazard ratio [HR], 1.69) in death-censored graft survival analysis (Table 4).

The reference transplant was defined by setting all covariates at median or most common values. BMI, body mass index; CI, confidence interval; CIT, cold ischemia time; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; OPO, Organ Procurement Organization; OR, odds ratio.

### Table 2

| Recipient BMI | Recipient height | CIT | Donor age | Donor eGFR | Pumped by OPO | OR    | 95% CI    | P      | 95% CI    |
|---------------|-----------------|-----|-----------|------------|---------------|-------|-----------|--------|-----------|
| 20            | 160             | 12  | 20        | 100        | Yes           | 0.1   | (0.05–0.19) | 48%    | (30%–66%) |
| 20            | 183             | 36  | 20        | 30         | No            | 2.59  | (1.61–4.16) | 96%    | (93%–98%) |
| 35            | 160             | 12  | 20        | 100        | Yes           | 0.23  | (0.13–0.43) | 67%    | (49%–81%) |
| 35            | 183             | 36  | 60        | 30         | No            | 13.99 | (8.71–22.49) | 99%    | (99%–100%) |
| 28            | 175             | 18  | 40        | 80         | Yes           | 0.53  | (0.31–0.93) | 83%    | (70%–91%) |

The reference transplant was defined by setting all covariates at median or most common values. BMI, body mass index; CI, confidence interval; CIT, cold ischemia time; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; OPO, Organ Procurement Organization; OR, odds ratio.
and having high creatinine (≥2.5) at discharge had a 49% higher risk-adjusted hazard of graft failure compared with the reference group. The elevated graft failure hazard for these patients was even higher (HR, 1.69) in death-censored graft survival analysis (Table 4). Figure 6 shows adjusted HRs for our primary exposures, the 4-level composite exposure of DGF (yes, no) and serum creatinine (≥2.5, <1.5) at discharge, on the 3 outcome variables (all-cause graft failure, death-censored graft failure, and patient mortality). Within each creatinine group and for all 3 outcomes, the HRs were statistically higher for recipients who experienced DGF compared with those who did not, suggesting the need for dialysis within the first week is an independent risk factor for long-term survival. Additionally, the DGF and creatinine interaction was not significant (P=0.62), suggesting that they were independently and additively associated with long-term all-cause graft survival. However, a careful examination of Figure 6 suggests the possibility of DGF by creatinine-at-discharge interaction effects for the other 2 outcomes: death-censored (P=0.02) and patient survival (P=0.09). Taken together, these results suggest that mild DGF is far less deleterious to both death-censored and all-cause graft failure compared with severe DGF. Figure 7 shows the Kaplan-Meier-based cumulative incidence curves for all-cause graft failure, death-censored graft failure, and patient mortality. The median graft survival was about 1 y greater for mild (9.5 y) versus severe (8.5 y) DGF. Moreover, DGF and creatinine of ≥2.5 (8.5 y) were associated with 2.6 y shorter graft survival versus no DGF and creatinine of <2.5 (11.1 y).

**DISCUSSION**

The primary reasons to prevent DGF are to avoid the expense, inconvenience, and last resort nature of dialysis, which exposes the graft to unnecessary risks such as hypotension,
thrombosis risk, increase in hospitalization, and poor clinical outcomes.\textsuperscript{24-26} By 2018, there were >500,000 US patients on maintenance dialysis, representing ~1% of the Medicare fee-for-service population but as much as 7.2% of Medicare fee-for-service spending.\textsuperscript{25} DGF incidence has risen despite the tapering of the “bolus effects” of KAS\textsuperscript{23} and DGF rates remain unacceptably high. Over the 15-y period studied, the rate of DGF in living donors declined, whereas there was a trend toward an increased incidence of DGF in deceased donors in the KAS era after 2014.\textsuperscript{23} Transplanting patients with longer time on dialysis post-KAS may explain the rise in DGF more than longer cold ischemia times.\textsuperscript{21} Additional factors include the increasing use of extended criteria donor kidneys to combat the organ shortage crisis, as well as organ allocation policies like KAS that have increased cold ischemia time and transplantation of recipients on longer dialysis times.\textsuperscript{23,27} The change to KAS to distribute organs primarily within large (250 nautical miles) circles instead of donor service areas seems to be associated with an additional, small increase in DGF rates.\textsuperscript{28} Currently, there are no approved therapies for treating DGF, although treatments targeting ischemic injury to prolong graft survival and outcomes are being tested in clinical trials. Although methods to predict DGF have been proposed, the numerous factors that can lead to DGF make it a challenge to accurately identify at-risk patients based on these factors. A meta-model combining 4 common predictive models for DGF after deceased donor transplantation showed that most models overestimate DGF incidence.\textsuperscript{29} The study identified 2 recipient parameters (cardiac function and preoperative diastolic blood pressure) that were not in previous models. Current predictive models have not been reliable or accurate and are not routinely used in clinical practice. Most models that perform well in the cohort in which they were discovered show lower predictive values when tested in external cohorts. Most models also tend

### TABLE 4. Influence of DGF and renal function at discharge on long-term, death-censored graft failure

| Risk factor | Hazard ratio | 95% confidence interval | P |
|-------------|--------------|-------------------------|---|
| Unadjusted results | | | |
| Non-DGF and creatinine ≥2.5 vs non-DGF and creatinine <2.5 | 1.23 | (1.10, 1.39) | <0.001 |
| DGF and creatinine <2.5 vs non-DGF and creatinine <2.5 | 2.08 | (1.99, 2.18) | <0.001 |
| DGF and creatinine ≥2.5 vs non-DGF and creatinine <2.5 | 1.56 | (1.49, 1.63) | <0.001 |
| Adjusted results | | | |
| Non-DGF and creatinine ≥2.5 vs non-DGF and creatinine <2.5 | 1.31 | (1.25, 1.37) | <0.001 |
| DGF and creatinine <2.5 vs non-DGF and creatinine <2.5 | 1.16 | (1.03, 1.31) | 0.014 |
| DGF and creatinine ≥2.5 vs non-DGF and creatinine <2.5 | 1.69 | (1.61–1.78) | <0.001 |

DGF, delayed graft function.

#### FIGURE 6. aHRs for primary exposure of DGF (yes, no) and serum creatinine (≥2.5, <1.5) at discharge, on the 3 outcome variables (all-cause graft failure, death-censored graft failure, and patient mortality). aHR, adjusted hazard ratio; DGF, delayed graft function.
to group DGF into 1 “catch-all” bucket without stratifying based on severity. A recent study stratifying DGF into 4 risk categories based on a simple frequency associated with the different risk scores of DGF showed that a hypothermic machine perfusion-based model had good discriminative power (c-statistic of 0.71) and identified DGF significantly better than flow rate and resistance. Because most studies define DGF dichotomously, we sought to advance the understanding of this early

FIGURE 7. Kaplan-Meier-based cumulative incidence curves for all-cause graft failure, death-censored graft failure, and patient mortality in DGF vs non-DGF recipients with creatinine of >2.5 mg/dL (severe DGF) and <2.5 mg/dL (mild DGF). DGF, delayed graft function.
outcome by delineating DGF severity based on serum creatinine at discharge. Though serum creatinine itself is an imperfect measure of renal function in dialysis patients, we found that in the context of measuring renal function among patients on dialysis before transplant, serum creatinine was virtually never so low as to misleadingly reflect “good” renal function. We show that over 99% of creatinine measurements for 44,638 KT candidates before transplant exceeded 2.5 despite administration of dialysis. Hence, we believe our use of creatinine of <2.5 at discharge is a reasonable, data supported, and useful proxy for “mild” DGF. Our results identified common donor factors that were associated with DGF, such as gender and BMI, but more importantly identified other factors, such as donor age, height, terminal eGFR, and pumping resistance as significantly predictive of DGF severity ($P < 0.001$). Studies have shown the association between body weight and the number of nephrons, specifically that decreased nephron numbers, being associated with hypertension and progression of renal disease. An association between donor age and the risk of DGF has also been shown with donor age <50 y, and the risk continued to be lower with decreased age. Similarly, in addition to recipient BMI and time on dialysis, we also discovered that recipient height was highly predictive of DGF severity ($P < 0.001$), with shorter stature conferring a large protective effect. Recipient height was inversely correlated with DGF and has been shown previously in a single-center study that associated extended criteria donor kidneys with decreased DGF. Several key recipient factors (eg, recipient height, pretransplant creatinine) not included in the well-known Irish DGF model account for differences in the clinical profiles we found to be associated with the odds of a DGF patient having mild versus severe DGF, vis-à-vis their likelihood of having DGF in the first place. Posttransplant, whether a DGF case is progressing toward severe DGF becomes evident as the need for dialysis continues, measures of renal function fail to improve, and other clinical explanations, such as hyperkalemia, are ruled out. Our modeling results provide a priori insights—before case progression—into which DGF recipients are more versus less likely to develop a severe case. Our hope is that the identification of recipients with higher odds of experiencing prolonged DGF may prove useful in guiding patient care, for example, in pretransplant deceased donor selection, as well as posttransplant DGF management such as induction therapy dose modification.

Our analysis established that DGF and creatinine at discharge were independently associated with long-term kidney recipient outcomes, but their effects differed depending on the target variable (graft function, death-censored graft function, and mortality). The c-statistic for our predictive models, both for DGF severity and posttransplant survival, ranged from 0.65 to 0.71 (moderately predictive) like previously published models. We also showed that median graft survival was 1 y greater after mild versus severe DGF. Additionally, DGF and creatinine ≥2.5 was associated with a decreased graft survival of ~2.6 y compared with no DGF and creatinine of <2.5 (Figure 6). The strength of our current analysis is the novel stratification of DGF severity based on creatinine at discharge, particularly because large cohort studies investigating DGF severity are scarce. We also describe how DGF stratified by severity is associated with graft and patient survival. We present the first step for a standardized method to assess DGF severity for further studies that can inform the selection process, treatment, and monitoring of transplanted kidneys at high risk for DGF. We would also like to acknowledge some limitations to our study. Creatinine at discharge as a measure of kidney function and its relation to DGF and acute kidney injury has been shown before in smaller studies; however, our rationale for stratification of DGF severity is novel as it is data driven (Figure 1). Although we used a dichotomous classification for severity, it is common in clinical studies, and we wanted to use it as a first step to investigate whether DGF severity affected clinical outcomes. Additionally, although the use of discharge creatinine may be an imperfect measure of renal function, the choice of 2.5 mg/dL as a threshold for mild DGF mitigates this concern because creatinine in end-stage renal disease patients on dialysis is virtually never this low. Our reasoning is supported by Figure 1, where >99% of patients who were on dialysis had a pretransplant creatinine value of >2.5 despite being on dialysis. Finally, we used creatinine at discharge in general as opposed to a fixed time point, but this was justified by correcting for LOS in the data. In fact, the need to rely on a proxy measure for DGF severity highlights an opportunity to improve OPTN data collection by adding new measures reflecting degrees of renal function immediately posttransplant and duration of dysfunction, instead of relying solely on the clinical decision to administer dialysis at least once during the first week.

In conclusion, we believe that the adverse cost, graft, and patient survival implications of severe DGF warrant additional investigation of these newly identified clinical factors to find ways to minimize the incidence of severe DGF and improve both kidney utilization and transplantation outcomes.

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