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A prediction model of delayed graft function in deceased donor for renal transplant: a multi-center study from China

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ABSTRACT

Background: Kidneys obtained from deceased donors increase the incidence of delayed graft function (DGF) after renal transplantation. Here we investigated the influence of the risk factors of donors with DGF, and developed a donor risk scoring system for DGF prediction.

Methods: This retrospective study was conducted in 1807 deceased kidney donors and 3599 recipients who received donor kidneys *via* transplants in 29 centers in China. We quantified DGF associations with donor clinical characteristics. A donor risk scoring system was developed and validated using an independent sample set.

Results: The incidence of DGF from donors was 19.0%. Six of the donor characteristics analyzed, i.e., age, cause of death, history of hypertension, terminal serum creatinine, persistence of hypotension, and cardiopulmonary resuscitation (CPR) time were risk factors for DGF. A 49-point scoring system of donor risk was established for DGF prediction and exhibited a superior degree of discrimination. External validation of DGF prediction revealed area under the receiver-operating characteristic (AUC) curves of 0.7552.

Conclusions: Our study determined the deceased donor risk factors related to DGF after renal transplantation pertinent to the Chinese cohort. The scoring system developed here had superior diagnostic significance and consistency and can be used by clinicians to make evidence-based decisions on the quality of kidneys from deceased donors and guide renal transplantation therapy.

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Introduction

Renal transplantation increases both the longevity and quality of life and is the gold standard of treatment for end-stage renal disease (ESRD) [1]. However, delayed graft function (DGF), a major early complication after renal transplantation, has seriously affected long-term survival of the recipients [2,3]. Among the many factors

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causing DGF, donor risks such as age and serum creatinine (sCr) level are crucial for donor and renal evaluation [4].

A pilot program of organ donation from deceased citizens initiated by the Chinese government has become the only source of deceased donors for renal transplantation since 2015 [5]. With the recent rapid increase in renal transpiration from deceased donors, the DGF rate after renal transplantation, especially from the high-risk donors, significantly increased [6,7] up to 25% in China, similar to that in the US [8,9]. The high rate of DGF significantly reduces the early recovery of the recipients and burdens both the hospitals and patients. Therefore, an understanding of the accurate evaluation of the donor, reasonable tradeoff on high-risk donor kidneys, and reduction of the DGF and primary non-function (PNF) incidence after renal transplantation is crucial.

The characteristics of the deceased donors determine the varying degrees of acute and chronic injuries that the donor kidneys may suffer from, which may influence the occurrence of DGF after renal transplantation [10]. International studies have established many donor assessment and DGF predictive models such as the kidney donor profile index and the model developed by Irish et al. [11,12]. However, the demographic characteristics and the primary pathogenesis of deceased Chinese donors may affect the accuracy of these criteria. No recognized evaluation criteria are currently available for deceased donors and organs in China. Our previous study revealed that age, cause of death, hypertension history, persistent hypotension duration, cardiopulmonary resuscitation (CPR), and terminal sCr before donation of the deceased donors were factors related to increased DGF incidence after renal transplantation in kidney transplant recipients [13]. However, the effects of these factors were not quantified. Additionally, the study had a single-center design and required its results to be further verified with more data from a multicenter study from different regions in China. Therefore, the present study attempted to collect and analyze data from different parts of China to preliminarily establish a quantitative and representative model for DGF prediction after renal transplantation and guidance for evaluation of deceased donors.

Materials and methods

Study cohort and ethics statement

The present multicenter, retrospective, observational cohort study was conducted in 1807 deceased donors and 3599 recipients in whom the donated renal were transplanted in 29 centers in China from November 2011 to March 2018.Donors above 16 years of age with confirmed identity; with no history of kidney diseases, diabetes, drug abuse, and uncontrollable psychotic symptoms; who were not actively infected with hepatitis B and C viruses, human immunodeficiency virus, bacteria, and fungi; and in whom the isolated renal had a warm ischemia time (WIT) <30 min and a cold ischemia time (CIT)<12 h were included in the study. At least one kidney from each donor was used for single renal transplantation. Recipients in the age range of 16–65 years, with body mass index (BMI) <28 kg/m^2, and with no history of renal transplantation were eligible for the study. Executed prisoners and recipients with multi-organ transplantation and ABO blood type incompatible renal transplantation were excluded from the study.

Additionally, information of deceased donors and renal transplant recipients in whom the surgery was performed at the First Affiliated Hospital of Xi'an Jiaotong University from May 2018 to April 2019 was also collected to validate the prediction value of our model.

Procurement of kidneys from all donors was conducted in accordance with the Declaration of Helsinki and the Declaration of Istanbul on Organ Trafficking and Transplant Tourism and approved by the Human Organ Transplantation and Ethics Committee of each institution. Organs were obtained by the Organ Procurement Organization (OPO) of each hospital and allocated by the China Organ Transplant Response System.

Immunosuppression regimen

All recipients were administered 1.25–1.50 mg·kg^{-1}·day^{-1} rabbit anti-thymocyte globulin (rATG; Genzyme Ireland, Waterford, Ireland) as intraoperative induction therapy and for 4–6 days postoperatively. A triple immunosuppressive regimen with enteric-coated mycophenolate sodium (EC-MPS; Myfortic, Novartis Pharma, Basel, Switzerland); prednisone; and calcineurin inhibitors (CNIs), including cyclosporine A (CsA; Sandimmun optoral, Novartis Pharma, Nuremberg, Germany) and tacrolimus (TAC; Prograf, Astellas Pharma, Deerfield, IL); was initiated postoperatively. The initial dosages of CsA, TAC, EC-MPS, and prednisone were 4.0–4.5 mg·kg^{-1}·day^{-1}, 0.06–0.08 mg·kg^{-1}·day^{-1}, 1080–1440 mg·day^{-1}, and 10–20 mg·day^{-1}, respectively.

Definitions of DGF and PNF

DGF was defined as the requirement for at least one dialysis session during the first week after renal transplantation, regardless of the clinical indication [14], except for non-donor related reasons such as acute rejection, ureteral thrombosis of renal graft and other recipient factors. Additionally, DGF developed in either one or both of the two kidneys from the same donor after transplantation was considered as DGF for that donor. PNF was defined as the failed functioning of the transplanted kidney that necessitated continued maintenance bydialysis6 months after renal transplantation recipients with DGF [15]. All observed DGF recipients were used for building the model.

Data collection

Baseline clinical donor demographics such as age, sex, BMI, terminal sCr, cause of death, hypertension history, persistent hypotension duration, and CPR were collected. Recipient variables such as age, sex, BMI, method, time and number of dialysis sessions during DGF, human leukocyte antigen (HLA) mismatches, panel reactive antibody (PRA), WIT as the time from cardiac arrest to cannula introduction, CIT, sCr levels at 1, 3, and 12 months after transplantation, duration of DGF, and graft survival at 1 year post-transplantation were recorded. Graft survival was defined as the recipient lived with a functional graft and without maintenance hemodialysis. Graft loss was defined as resumption of maintenance dialysis, eGFR less than 10 $mL \cdot min^{-1} \cdot (1.73\ m^2)^{-1}$, and graft excision or re-transplantation.

Development and validation of DGF risk prediction model

In our study, the donor was used as the basic unit, and the endpoint was defined as at least one recipient developed DGF. The observed endpoint was 'DGF donor', otherwise it was 'non-DGF donor'. The observed endpoint was 'DGF donor', otherwise it was 'non-DGF donor'. Risk factors identified for inclusion of multivariate Logistic regression analysis were those shown to be contributing factors important DGF risk predictors in the univariate Logistic regression and our previous study [13]. In addition, factors chosen were those easily measured by widely available, noninvasive clinical tests. Development of the risk score had two steps. First, a Cox proportional hazards model was used to estimate the β regression coefficient, p value, and odd ratio and its 95% CI for each of the selected risk predictors. Second, a donor rating scale was constructed based on the regression coefficient of each factor at different levels as β value in the multivariate Logistic regression model. The regression coefficient of each risk predictor was multiplied by 10 times and was rounded into an integer value to generate the risk score [16].

In addition, the DGF risk prediction model was validated using another independent sample by assessing its discrimination with the receiver-operating characteristic (ROC) curve, area under ROC (AUROC) curve, sensitivity, and specificity. Calibration curves were plotted to assess the calibration of the prediction nomogram, accompanied with the Hosmer-Leme show test to determine consistency of the model. A poor test-retest reliability ($p < .05$) implies that the model does not calibrate perfectly. We also collected observed DGF incidence for six patient groups in the validation cohort with the same cumulative DGF risk scores section. Observed DGF incidences were plotted against the mean predicted risk in the group to form a calibration chart [16].

Statistical analysis

Continuous variables with normal distribution were expressed as means ± standard deviation, and categorical variables were expressed as frequencies and percentages. Differences in the clinical characteristics between recipients and donors were examined using the Student's t test for continuous variables and the chi-square test for discrete variables. All statistical analyses were performed using SPSS for Windows (version 20.0, IBM Corp., Armonk, NY). A p value of $< .05$ was considered statistically significant.

Results

Characteristics of the donors and recipients

The study comprised 1807 donors and 3599 recipients. Of the 1807 donors, one kidney each in 15 donors was discarded for non-renal functional reasons such as contusion, vascular injury, and capsule damage. A total of 167 cases were excluded from this study due to missing data. Tables 1 and 2 present the qualitative and quantitative variables of donors and recipients. The mean age of donors was 38.9 ± 16.8 years, with 38.30%of donors being older than 50 years. The mean terminal sCr of donors was 104.4 ± 87.0 μmol/L; the mean duration of CIT and WIT was 6.2 ± 3.2 h and 15.3 ± 4.4 min, respectively; and the mean BMI was 22.0 ± 3.7 kg/m^2. Of the 1807 donors, 83.7% were men, 50.9% died from brain trauma,38.3% died from cerebral hemorrhage, 22.5%

Table 1. Baseline characteristics of donors in the DGF and non-DGF groups.

Variable		Non DGF ($n = 1464$)	DGF ($n = 343$)	p Values
Age (years)		39.3 ± 18.2	38.8 ± 16.4	.617
16–40		541 (37.0%)	90 (26.2%)	.001
40–49		388 (26.5%)	96 (28.0%)	
50–64		483 (32.9%)	137 (40.0%)	
≥65		52 (3.6%)	20 (5.8%)	
Gender				
Female		248 (17.0%)	54 (15.7%)	.590
Male		1216 (83.0%)	289 (84.3%)	
BMI (kg/m^2)		22.1 ± 4.4	22.0 ± 3.5	.768
Primary disease-				
Cerebral trauma		789 (53.9%)	131 (38.2%)	<.001
Cerebral hemorrhage		519 (35.5%)	173 (50.4%)	
Hypoxic ischemic encephalopathy		62 (4.2%)	18 (5.32%)	
Others		94 (6.4%)	21 (6.1%)	
Hypertension course (years)				
None		1203 (82.2%)	198 (57.7%)	<.001
0–4		138 (9.4%)	62 (18.1%)	
5–9		78 (5.3%)	62 (18.1%)	
≥10		45 (3.1%)	21 (6.1%)	
Cardiopulmonary resuscitation (min)				
none		1416 (96.7%)	281 (81.9%)	
0–9		13 (0.9%)	39 (11.4%)	<.001
10–29		22 (1.5%)	14 (4.1%)	
≥30		13 (0.9%)	9 (2.6%)	
Creatinine (μmol/L)		$n = 1412$	$n = 332$	
<177		1255 (85.7%)	247 (74.4%)	<.001
177–265		89 (6.3%)	42 (18.1%)	
265–442		59 (4.2%)	29 (8.7%)	
>442		9 (0.6%)	14 (4.2%)	
Hypotension persistent (min)				
None		1349 (92.1%)	281 (81.9%)	
SBP < 80mmHg	SBP < 50mmHg	–	–	–
<60	<10	87 (6.0%)	44 (12.8%)	<.001
≥60	≥10	28 (1.9%)	18 (5.3%)	

DGF: delayed graft function; BMI: body mass index; SBP: systolic blood pressure.

Table 2. Baseline characteristics of the recipients in the DGF and non-DGF groups.

Variable	DGF ($n = 479$)	Non-DGF ($n = 3120$)	p Values
Age (years)	40.4 ± 10.5	39.7 ± 10.7	.454
Gender			
Female	159 (33.2%)	1040 (33.3%)	.948
Male	320 (66.8%)	2080 (66.7%)	
BMI (kg/m^2)	21.1 ± 3.4	19.9 ± 3.1	.061
Dialysis method			
Hematodialysis	438 (91.4%)	2848 (91.3%)	
peritoneal dialysis	41 (8.6%)	272 (8.7%)	
Dialysis time (months)	19.3 ± 8.8	17.9 ± 10.1	
HLA mismatches	2.5 ± 1.3	2.4 ± 1.3	.633
PRA			
Negative	403 (84.1%)	2576 (80.7%)	.117
≤5%	51 (10.6%)	322 (10.3%)	
5–50%	20 (4.2%)	129 (4.1%)	
≥50%	5 (1.0%)	93 (3.0%)	
WIT (min)	16.1 ± 4.9	14.9 ± 4.2	.696
CIT (h)	6.4 ± 3.3	5.9 ± 2.6	.367

DGF: delayed graft function; BMI: body mass index; HLA: human leukocyte antigen; PRA: panel reactive antibody; WIT: warm ischemia time; CIT: cold ischemia time.

had history of hypertension, 9.8% suffered from hypotension, and 6.1% received CPR.

The mean age of the recipients was 41.7 ± 13.3 years, the mean BMI was 21.0 ± 3.2 kg/m^2, and the mean HLA mismatches were 2.5 ± 1.7. Of the 3599 recipients, 66.8% were men, and 17.2% had a positive PRA.

DGF and renal function

Out of the 3599 recipients and 1807 donors, 479 (13.3%) recipients who had received transplants from 343 (19.0%) donors developed DGF after renal transplantation, whereas PNF developed in 69 (1.9%) recipients and 43 (2.4%) donors. Of these, DGF occurred in both transplanted kidneys of 136 donors, in one of two transplanted kidneys of 207 donors, and in one transplanted kidney where the kidney on the other side was rejected in 15 donors. PNF occurred in both transplanted kidneys of 26 donors, in one of two transplanted kidneys in 17 donors, and in one transplanted kidney where the contralateral kidney was rejected in 15 donors.

The mean duration of DGF was 22 (17–34) days, with a mean dialysis time of 5.8 ± 5.9 years. The 1-year survival rates of DGF and non-DGF renal grafts were 93.3% and 95.8%, respectively. The Kaplan-Meier curve of renal graft survival between recipients exhibiting DGF

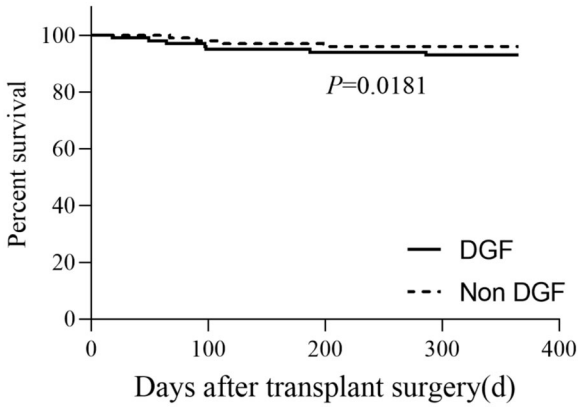

Figure 1. The Kaplan-Meier curve of renal graft survival in DGF and non-DGF groups ($p = .018$).

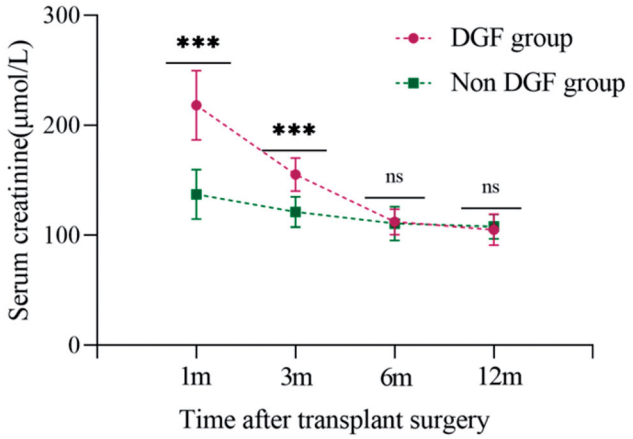

Figure 2. Serum creatinine levels between DGF and non-DGF renal grafts at different time points at 1 year after renal transplantation. $^{***}p < 0.001$ vs. non DGF group.

and recipients without DGF showed statistically significant difference ($p = .018$) (Figure 1).

After excluding PNF, the sCr level in recipients exhibiting DGF was significantly higher than that in recipients without DGF at 1 and 3 months post-transplantation ($p < .001$). However, this difference was not statistically significant at both 6 and 12 months post-transplantation ($p = .543$ and $p = .248$, respectively; Figure 2).

Risk factors of donor related to DGF

Significant differences were observed in the primary disease, hypertension course, sCr, persistent hypotension, and CPR time between DGF-and non-DGF-related donor groups (Table 1, $p < .05$). Although no significant difference was observed in the mean age between DGF- and non-DGF-related donor groups ($p = .623$), the distribution of donor age in the DGF-related group was significantly different from that in the non-DGF-related group ($p = .001$). The highest incidence of DGF (28%) was observed in donors above 65 years of age. Additionally, no significant difference was observed in the BMI and gender distribution between the DGF- and non-DGF-related donor groups ($p = .764$ and .590, respectively).

The univariate logistic regression analysis demonstrated that age, primary diseases, hypertension history, sCr level, persistent hypotension duration, and CPR time of donors were risk factors for DGF (Table 3). The DGF incidence increased from 14 to 28% with increase in the age of donors and was significantly higher in donors with history of hypertension than in donors without history of hypertension (36% *vs.* 14%, $p < .001$). The DGF incidence increased with a prolonged history of hypertension. Among primary diseases, the incidence of DGF was the highest (25%) in donors with cerebral hemorrhage, whereas it was the lowest (14%) in donors with cerebral trauma. Furthermore, the DGF incidence increased from 17 to 56% in donors without history of CPR and with CPR history, respectively ($p < .001$). The DGF incidence also increased from 16% to 35% with an increase in the terminal sCr level of donors ($p < .001$), and from17 to 35% in donors without hypotension and with persistent time and degree of hypotension, respectively ($p < .001$). It increased with an increase in the severity of hypotension.

Development of DGF risk prediction model

A DGF risk prediction model was established using univariate and multivariate logistic regression modeling techniques. Table 3 presents the final modeling results of the model. The univariate analysis results exhibited that six donor factors, namely age, primary diseases, hypertension course, sCr level, persistence of hypotension, and CPR time were significantly associated with DGF incidence. Table 3 presents the results of the multivariate analysis of the six factors and the final DGF risk prediction model.

Performance of the DGF risk prediction model

Data of the deceased donors and renal transplant recipients, whose surgery was performed at the First Affiliated Hospital of Xi'an Jiaotong University from May 2018 to April 2019, were further independently analyzed to validate the clinical and prediction performance of our model using the established final model. The ROC curve and logistic regression model analyses exhibited an AUC of 0.7552 (95%CI: 0.67–0.84). The optimal operation point (with the maximum Youden's index) of this DGF risk prediction model was 0.38, with a sensitivity of 75.7% and a

Table 3. Regression analysis of DGF risk from donor and the donor risk predictive score.

		Univariate regression		Multivariate regression			
Factors		OR (95%CI)	*p* Values	OR (95%CI)	*p* Values	β	Scores
Age (years)							
16–39		–	–	–	–	–	0
40–49		1.26 (0.89,1.80)	0.131	1.20 (0.79,1.71)	0.433	0.14	1
50–64		1.38 (0.96,1.97)	0.077	1.25 (0.84,1.84)	0.261	0.22	2
≥65		1.42 (1.09,1.84)	0.009	1.36 (0.86,2.17)	0.191	0.31	3
Primary disease							
Cerebral trauma		–	–	–	–	–	0
Cerebral hemorrhage		1.94 (1.51,2.5)	<0.001	1.33 (0.96,1.84)	0.081	0.28	3
Hypoxic ischemic encephalopathy		2.10 (1.27,3.39)	0.003	1.82 (1.06,3.01)	0.024	0.59	6
Others		1.42 (0.89,2.19)	0.129	1.34 (0.83,2.12)	0.221	0.29	3
Hypertension (years)							
None		–	–	–	–	–	0
0–4		2.29 (1.62,3.21)	<0.001	1.65 (1.09,2.48)	0.017	0.49	5
5–9		2.4 (1.55,3.66)	<0.001	1.83 (1.11,2.98)	0.016	0.60	6
≥10		2.75 (1.55,4.76)	<0.001	1.98 (1.04,3.66)	0.032	0.68	7
Cardiopulmonary resuscitation (min)							
None		–	–	–	–	–	0
0–9		3.53 (1.15,10.22)	0.020	1.68 (0.45,5.64)	0.414	0.51	5
10–29		3.45 (1.53,7.54)	0.002	1.94 (0.76,4.68)	0.149	0.66	7
≥30		3.33 (2.02,5.42)	<0.001	2.24 (1.3,3.79)	0.003	0.80	8
Creatinine (μmol/L)							
<177		–	–	–	–	–	0
177–265		2.46 (1.67,3.60)	<0.001	2.04 (1.08,3.73)	0.023	0.71	7
265–442		2.58 (1.58,4.13)	<0.001	2.78 (1.55,7.40)	0.005	0.79	8
>442		16.10 (5.73,57.12)	<0.001	9.82 (1.22,88.68)	0.020	1.73	17
Hypotension course (min)							
None		–	–	–	–	–	0
SBP < 80mmHg	SBP < 50mmHg						
<60	<10	2.66 (1.71,4.06)	<0.001	1.61 (1.17,2.39)	0.005	0.52	5
≥60	≥10	5.48 (2.65,11.25)	<0.001	2.70 (1.55,4.60)	<0.001	0.77	8

DGF: delayed graft function; OR: odds ratio; CI: confidence interval; SBP: systolic blood pressure.

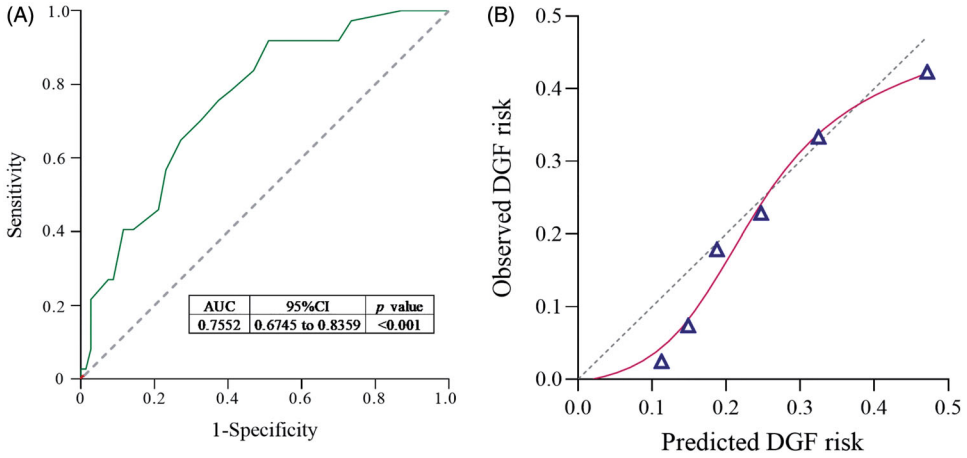

Figure 3. External validation of the DGF risk predictive model from donors ($n = 260$). (A) Discrimination ability of the model determined by receiver-operating characteristic (ROC) curve. (B) Consistency check of the model.

specificity of 62.6% (Figure 3(A)). The actual DGF incidence was close to the predicted DGF incidence with the slope and intercept being 1.012 and 0.035, respectively. A calibration chart for predicted DGF risk and observed DGF risk with a correlation coefficient of 0.734, showing a good correlation in the our DGF risk model (Figure 3(B)).

Moreover, of the 260 analyzed renal transplant cases, the DGF scores of all donors were divided into six categories: 0–5, 5–10, 10–15, 15–20, 20–25, and >25 points. The DGF incidence increased with the increase in donor DGF score and was significantly different among donors at different score categories ($p = .034$). The difference in the DGF duration among donors at different score categories was statistically non-significant ($p = .068$). The time of renal graft recovery in recipients not exhibiting DGF was significantly prolonged, with DGF scores of up to 20 points ($p = .035$; Table 4).

Table 4. DGF and renal graft recovery between different donor DGF risk score stages in external validation.

DGF donor risk score (points)	0–10	10–20	20–30	≥30	*p* Values
N	141	105	13	1	
DGF, n (%)	13 (9.2%)	29 (27.6%)	10 (76.9%)	1 (100%)	.034
DGF duration (days)	20 (9,28)	24 (17,32)	29 (23,39)	N/A	.068
Recovery time of non-DGF renal graft (days)	4 (3,7)	6 (5,9)	11 (9,19)	N/A	.035

DGF: delayed graft function.

Disscussion

In 2011, the Chinese Ministry of Health published the following classification of donor after cardiac death (DCD) [25], which is referred to as the 'Chinese Standard of DCD'. Chinese Class I (C-I) corresponds to international standard donor after brain death (DBD) organ donation. After strict medical examination, clinical brain death is definitively diagnosed by qualified experts. Once brain death is determined, treatment is discontinued and the donor's organs are donated with the informed consent of the family members; China Class II (C-II) corresponds to international DCD organ donation; China Class III (C-III) corresponds to the transitional period of both brain and heart death organ donation (donation after brain death awaiting cardiac death, DBCD). Due to the uniqueness of China's national conditions, most donations fall into this category. There is no legislation for brain death in China; thus, family members may disagree with organ donation before the donor's heart has stopped beating, even when the donor meets the criteria of brain death. In this case, the donation should follow the donation procedure for Maastricht class III DCD donors, i.e., where cardiopulmonary support is removed in a stepwise manner, and donation is performed after cardiac arrest occurs.

The objects of this study are deceased donors. China has an opt-in system, i.e., only those who have given explicit consent are donors. In China, there are two types of informed consent to use organs from deceased donors: (i) where the deceased has expressed a willingness to be an organ donor either in a living will or elsewhere in writing; (ii) when the patient's closest relative provides written consents for organ donation, provided that the potential donor had not expressed opposition to donation prior to death. Most donations by citizens with unknown willingness are cases where the family members opt in for organ donation. All cases of organ donation must be approved by all the immediate family members of the donor with signed written informed consents.

Even if most of the renal grafts of recipients with DGF recover from DGF, the 1-year renal graft survival among these recipients is decreased [17]. The post-transplantation incidence of DGF increased with the deceased donor risks. Deceased donors commonly exhibit more than one risk factor simultaneously, and these risk factors could interact with each other. Thus, we performed multivariate analysis to objectively and accurately predict DGF risk. The weighting coefficient of each risk factor was determined at different stratification, and a 49-point score donor risk system was established for DGF prediction with a good degree of discrimination. The established DGF risk prediction model allowed the selection of the deceased donor for renal transplantation with reference value and could be used for DGF prediction before organ donation and procurement. The model can thus be clinically applied for patient selection and determination of the suitability of the donor kidney for transplantation.

Among the independent risk factors of DGF, terminal sCr, persistence of hypotension, and CPR are useful for optimizing donor management and improving graft outcomes. Donor age, primary disease, and history of hypertension could help physicians predict potential renal injury. High terminal sCr, hypotension persistence, and history of CPR in donors could increase DGF risk by3–6folds, implying that the kidney might suffer acute injury and there by result in an increased incidence of DGF. Asher et al. Demonstrated that CPR could adversely affect the transplanted kidney [18]. Furthermore, renal ischemia/reperfusion injury mediated by vasoactive drugs and CPR could cause functional impairment through multiple factors such as renal vasoconstriction and tubular obstruction, and inevitably cause DGF after renal transplantation [19]. Moreover, a Chinese multicenter study with a small sample size also observed that CPR and the use of vasoactive drugs for the treatment of hypotension in the deceased donor were independent risk factors of DGF. This finding was consistent with our study [20]. The present study exhibited that the hypertension history of different periods presented with a comparable DGF risk (from 2.29- to 2.75-fold). Data from the United Network for Organ Sharing exhibited that long-standing (10 years) donor hypertensive history was associated with significantly decreased recipient graft survival, whereas recent hypertensive history (less than 10 years) was apparently not detrimental [21]. This discrepancy may be explained by the difference in public awareness about the control of hypertension in the Chinese and

American cohorts. Primary diseases were also confirmed as a risk factor for DGF. Hypoxic ischemic encephalopathy exhibited the highest DGF risk, increasing the possibility of DGF by 2.1-fold compared with cerebral trauma. This finding can be explained by the fact that the kidneys of donors with hypoxic ischemic encephalopathy usually suffered from acute injury caused by ischemia hypoxia. The present study demonstrated that donor age was not a sensitive factor for clinical decision because the risk of DGF could increase by 1.42-fold in kidneys of donors above 65 years of age. This is concurrent with the fact that the percentage of sclerotic glomeruli in the human kidney varies between 0.2 and 16.7% at an age of 55 years, and between 1.5 and 23.0% at an age of 75 years, suggesting that it would be inappropriate to abandon donors based on age alone [22,23].

Several factors, related to donors, recipients, and even the process of renal procurement and storage, are associated with DGF risk. We eliminated all other risk factors in the study to objectively and accurately reflect the relationship between donors and the risk of DGF. WIT and CIT were two previously reported risk factors for DGF [24]. Although many donors in our study presented with brain death, they could not be included in the study as donor after brain death had not been legislated in China. A novel donation concept of organ donation in brain death followed by circulatory death was officially initiated in China in 2011 and could be regarded as a controlled circulatory death [25]. Moreover, the donated organs were distributed to nearby transplantation centers through the OPO according to the China Organ Transplant Response System. Thus, the WIT and CIT were quite short in our study as donation after cardiac death which included the influence on DGF from them. Additionally, some donor risk factors such as diabetes history, which is known to be associated with DGF, were not included in our study [26]. However, the number of diabetic donors was small, and only accounted for 1.9% of the total rejected kidneys for transplantation. Therefore, diabetic donors were excluded in our study. Trauma and cerebral hemorrhage were the major causes of death in our study, accounting for 89% of total cases. Diabetes is rare in cases with cerebral hemorrhage and trauma. Kidneys from children and teenager donors exhibited a high incidence of surgical complication when transplanted in adults [27]. Therefore, donors below 16 years of age were also excluded in our study to eliminate this non-donor confounding factor for DGF. Our statistical results exhibited that DGF occurred in both donated kidneys and the only available kidney of 45% donors, and in only one kidney of two donated kidneys of 55% donors. Additionally, all recipients with DGF underwent dialysis at least twice after transplantation. The incidence of DGF in one kidney must be considered as a risk factor when considering the transplantation of the contralateral kidney in a recipient. Two people may react differently to the risk factor of DGF in the donor, causing different results for DGF. Therefore, the model offers the choice of a recipient who might better tolerate dialysis after transplant or rejection of the kidney for transplant. Furthermore, we also speculated that the difference of DGF between two renal grafts from the same donor might be related to the different pathophysiological development of the human body. The pathological mechanisms underlying the differences between the two kidneys from the same donor must be further explored.

Studies have demonstrated the donor scoring systems are beneficial for improving the outcomes of the transplanted kidneys (including DGF) for the deceased donor [28,29]. Among these models, the model developed by Irish et al. in 2010 was reported to have good discrimination and perfect calibration for the Chinese cohort and was most associated with the observed DGF incidence [12,30]. The model developed by Irish et al. comprised 13 factors including both donors and recipients, and its operation process was relatively complicated. Furthermore, some variables in their model such as 'whether the recipient is black' do not apply to Chinese patients, which may influence the predictive value of DGF [12]. Additionally, other prediction models, such as the Zaza 2015 and Chaphal 2014 models, have lower predictive values than the model developed by Irish et al. (2010) [30–32]. So Far, there was no DGF prediction model of Chinese deceased donor due to the differences in the demographic characteristics, disease structures, medical conditions, and other aspects between Europe or America and China, the DGF predictions established abroad could not reflect the characteristics of the Chinese cohort. Our model is more relevant to the characteristics of the Chinese cohort. Moreover, different inclusion and exclusion criteria used in our study and the study of Irish et al. would lead to a population bias, which could explain the differences observed between that study and ours. Our model is more relevant to the characteristics of the Chinese cohort. The results of the external validation demonstrated that our model could effectively predict the DGF incidence in transplanted kidneys from deceased Chinese donors; however, it could not predict the severity of DGF. Other than the donor risk factors, the duration and prognosis might be affected by the condition

of recipients with DGF due to immunosuppressive therapy and rejection after renal transplantation [6]. Therefore, our model could not accurately predict the duration of DGF. Our results also exhibited that the time of renal graft recovery was positively correlated with the donor risk score, which might reflect the quality of the kidney to some extent. High DGF incidence was observed in the category with >20 points, especially when this was >30. Since most kidneys of donors with >30 scores were discarded, the result was obtained from a small sample size. Studies with a larger sample size must be conducted to verify our findings.

The present study has several limitations. First, the independent patients, whose data were used to plot the ROC curve to validate our model, were from the same transplantation center. Additionally, other confirmed predictive factors such as diabetes were not recognized in our study due to the insufficient sample size. Therefore, further external multicenter validation with a large sample is required. Moreover, our model was established based on the deceased Chinese donor. Its utilization in other ethnicities must be further explored.

Therefore, our study determined the deceased donor risk factors related to DGF after renal transplantation pertinent to the Chinese cohort and developed an effective scoring system for DGF prediction in the Chinese cohort. The scoring system included six factors, namely donor age, primary diseases, hypertension history, terminal sCr, hypotension persistence, and CPR time. The scoring system had superior diagnostic significance and consistency and can be used by clinicians to make evidence-based decisions on the use of kidneys from deceased donors and guide renal transplantation therapy.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University (XJTU1AF2015LSL-058). The study was performed in accordance with the ethical standards put forth by the Declaration of Helsinki.

Disclosure statement

All authors declare that they have no conflict of interests.

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Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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