Predictive Score Model for Delayed Graft Function Based on Hypothermic Machine Perfusion Variables in Kidney Transplantation

Chen-Guang Ding1,2, Yang Li1,2, Xia-Hui Tian1,2, Xiao-Jun Hu1,2, Pu-Xun Tian1,2, Xiao-Ming Ding1,2, He-Li Xiang1,2, Jin Zheng1,2, Wu-Jun Xue1,2

1Department of Kidney Transplantation, Nephropathy Hospital, The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, Shaanxi 710061, China
2Institute of Organ Transplantation, Xi’an Jiaotong University, Xi’an, Shaanxi 710061, China

Abstract

Background: Hypothermic machine perfusion (HMP) is being used more often in cardiac death kidney transplantation; however, the significance of assessing organ quality and predicting delayed graft function (DGF) by HMP parameters is still controversial. Therefore, we used a readily available HMP variable to design a scoring model that can identify the highest risk of DGF and provide the guidance and advice for organ allocation and DCD kidney assessment.

Methods: From September 1, 2012 to August 31, 2016, 366 qualified kidneys were randomly assigned to the development and validation cohorts in a 2:1 distribution. The HMP variables of the development cohort served as candidate univariate predictors for DGF. The independent predictors of DGF were identified by multivariate logistic regression analysis with a P < 0.05. According to the odds ratios (ORs) value, each HMP variable was assigned a weighted integer, and the sum of the integers indicated the total risk score for each kidney. The validation cohort was used to verify the accuracy and reliability of the scoring model.

Results: HMP duration (OR = 1.165, 95% confidence interval [CI]: 1.008–1.360, P = 0.043), resistance (OR = 2.190, 95% CI: 1.032–10.20, P < 0.001), and flow rate (OR = 0.931, 95% CI: 0.894–0.967, P = 0.011) were the independent predictors of identified DGF. The HMP predictive score ranged from 0 to 14, and there was a clear increase in the incidence of DGF, from the low predictive score group to the very high predictive score group. We formed four increasingly serious risk categories (scores 0–3, 4–7, 8–11, and 12–14) according to the frequency associated with the different risk scores of DGF. The HMP predictive score indicates good discriminative power with a c-statistic of 0.706 in the validation cohort, and it had significantly better prediction value for DGF compared to both terminal flow (P = 0.012) and resistance (P = 0.006).

Conclusion: The HMP predictive score is a good noninvasive tool for assessing the quality of DCD kidneys, and it is potentially useful for physicians in making optimal decisions about the organs donated.

Key words: Delayed Graft Function; Donation after Cardiac Death; Hypothermic Machine Perfusion; Kidney Transplantation

Introduction

Donation after cardiac death (DCD) is becoming the main source of organ transplantation in China.1,2 The high incidence of delayed graft function (DGF) and the higher risk of early graft dysfunction and failure were the main concerns of DCD kidney transplantation.3,4,5 Hypothermic machine perfusion (HMP) is used to reduce the incidence of DGF and to ameliorate the transplantation of renal function by decreasing the ischemic damage of DCD kidneys that occurs in static cold storage.6,7 In addition to possible therapeutic benefits, HMP provides a choice for assessing kidney viability that is essential for optimal organ allocation.8,9,10 An accurate assessment of the quality...
of the kidneys may reduce the number of kidneys discarded and the number of poor kidney transplants, resulting in an unacceptable survival rate. Kidney biopsy has been used as the gold standard for assessing kidney quality before transplantation until now. However, a kidney biopsy is a time-consuming and invasive process that requires experienced pathologists to assess the kidney quality. Therefore, several predictive models for DGF have been developed within the last few years.

However, many factors that are not included in these donor models may affect the kidney quality such as inflammatory lesions caused by brain death, hemodynamic instability during donor hospitalization, traumatic damage caused during organ procurement, and renal ischemic injury in the course of transport. Many transplant centers have assessed the quality of DCD kidneys through HMP parameters. One study further analyzed the Eurotransplant trial that showed that terminal resistance was an independent risk factor for DGF; however, the ability to predict terminal resistance was low with a c-statistic score of 0.58.

Although the authors of the trial oppose the use of HMP parameters as criteria for kidney rejection, high terminal resistance and low terminal flow rate have been associated with higher rates of rejection. In summary, it is still controversial whether a single HMP parameter can predict DGF and assess kidney viability and allograft outcomes after renal transplantation. We believe that the combination of all HMP factors should be more predictive value of DGF than a single HMP factor. Therefore, we applied the method of Sullivan et al. to convert the model of HMP variables to a simple point system. The risk score was derived from a competing risk model with DGF. To calculate the risk score, points for all factors were summed up.

The objectives of this study were to use a readily available HMP variable to design a scoring model that could identify the highest risk of DGF and provide guidance and advice for organ allocation and DCD kidney assessment.

Methods

Ethical approval

This retrospective, observational cohort study was approved by the Ethics Committee of the First Affiliated Hospital of Xi’an Jiaotong University. All patients provided informed consent. This was in compliance with the provisions of the current Declaration of Helsinki principles and good clinical practice guidelines. The kidney grafts were provided by the Coordination Group of Shaanxi Red Cross Organization and harvested from DCDs classified as controlled or uncontrolled DCDs according to the Maastricht classification. No touch time in donor patients after cardiac death was defined as 2–5 min before the heart stops beating, according to Chinese regulatory institutions. None of the organs in this study were obtained from a vulnerable population, and there were no ethical or legal conflicts.

Study design

The age of the recruited patients ranged from 16 to 65 years old. They underwent primary kidney transplantation with HMP-preserved DCD kidneys from September 1, 2012, to August 31, 2016. Patients were excluded from the study if (1) they had undergone retransplantation or had accepted organs other than the kidneys; (2) had a positive crossmatch or positive panel-reactive antibody (PRA); and (3) had hepatitis, active infection, or abnormal hepatic function. DCD donor inclusion criteria were as follows: (1) identity, (2) negative HIV antigen test, (3) 16 years ≤ aged <65 years, and (4) negative diagnosis for the conditions of malignant tumor, drug abuse, or renal diseases. Qualified kidneys were randomly assigned to the development and validation cohorts using a 2:1 distribution generated by a Web-based program (www.randomization.com). The diagnostic criterion of DGF was dialysis needed in the 1st-week posttransplant.

Hypothermic machine perfusion

After being procured and trimmed, all kidneys used LifePort (Organ Recovery Systems, Chicago, IL, USA) for continuous perfusion preservation with an initial pump pressure of 30 mmHg (1 mmHg = 0.133 kPa). The machine continuously recorded the perfusion parameters (pressure, temperature, resistance, flow, and duration).

Immunosuppressive regimen

A triple immunosuppressive regimen consisting of mycophenolic acid (MPA), calcineurin inhibitor (CNI), and prednisone was used as the initial regimen in all patients. MPA is enteric-coated mycophenolate sodium or mycophenolate mofetil. CNI is tacrolimus or cyclosporin A. All recipients were induced with rabbit antithymocyte globulin (Thymoglobuline; Genzyme, Waterford, Ireland; 1.25 mg·kg⁻¹·d⁻¹ on days 0 and 2 up to day 4 after transplantation).

Statistical analysis

The HMP variables of the development cohort were used as candidate univariate predictors for DGF, and the independent predictors of DGF were identified using multivariate logistic regression analysis. Using the estimated odds ratios (ORs) from the multivariate logistic regression analysis model and the integer 1 was assigned to each OR value of 1. A total of 1000 bootstrap samples were selected from the development cohort to avoid overfitting the data. For each sample, the step-by-step selection procedure was used to select the independent predictor of DGF. The variables selected in ≥90% of the boot model were included in the final multivariate model. The predictive ability of the risk score was assessed by a c-statistic of the receiver operator characteristic curve (ROC), and the calibration was evaluated by Hosmer-Lemeshow Chi-squared statistic. A P < 0.05 was considered statistically significant. All calculations were performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA).
RESULTS

Demographic and clinical characteristics

A total of 366 qualified patients were randomly assigned to the development cohorts (n = 244) and the validation cohorts (n = 122), respectively. In the two groups, 117 donors were the same. Table 1 showed their demographic and clinical characteristics. There were no significant differences between the two groups with respect to donor and recipient ages, duration of dialysis pre-transplant, positivity for PRA, number of HLA mismatches, cold ischemic time, warm ischemic time, primary diseases of the recipients, causes of death of the donors, and donors’ serum creatinine levels and body mass index.

Graft and patient survival rates

By the one-year follow-up assessment, seven patients (including two cases of none-recovery AMR, one case of primary nonfunctioning, two case of renal artery stenosis, and two case of ureteral obstruction in transplanted kidney) in the development cohorts and four patients (two cases of none-recovery AMR, one case of transplanted kidney rupture, and one case of renal allograft abscess) in the validation cohorts had developed allograft failure. In the same period, five patients in the development cohorts (including two patients died from cardiovascular disease and three from pulmonary infection) and three patients in the validation cohorts (including one patient died from cardiovascular disease, one from a traffic accident, and one from pulmonary infection) had died. Both the allograft survival (97.1% vs. 96.7%, χ² = 0.020, P = 0.895) and the patient survival (98.0% vs. 97.5%, χ² = 0, P = 0.902) rates at 1-year follow-up were similar between the two study groups.

Hypothermic machine perfusion parameters

The HMP variables of the following: terminal flow, terminal resistance, temperature, pump pressure, and HMP duration did not differ between the two groups [Table 2].

Univariate and multivariate analyses of hypothermic machine perfusion variables associated with delayed graft function

Univariate analysis clearly showed that the HMP variables, such as the terminal flow (OR = 0.863, 95% confidence interval [CI]: 0.729–0.969, P < 0.001) and the terminal resistance (OR = 7.262, 95% CI: 2.909–15.508, P < 0.001), were significantly related with DGF onset. Dichotomous cut-points for HMP duration showed statistically significant association as compared to the continuous variable: kidneys with HMP duration of <12 h had a significantly higher DGF rate as compared to kidneys with an HMP

| Table 1: Demographic and clinical characteristics of donors and recipients in the development and validation cohorts |
|---------------------------------------------------------------|
| **Variables**                                                      | Development cohort | Validation cohort | t or χ² | P     |
| Recipients                                                       | n = 244            | n = 122           |        |       |
| Age (year)                                                       | 36.5 ± 10.5         | 35.8 ± 9.8        | 0.629* | 0.510 |
| Gender (male/female), n                                          | 164/80             | 83/39             | 0.020* | 0.875 |
| BMI (kg/m²)                                                     | 20.5 ± 3.3          | 20.8 ± 3.0        | 0.845* | 0.569 |
| Hemodialysis, n (%)                                              | 225 (92.1)          | 112 (91.8)        | 0.020* | 0.891 |
| Dialysis duration (days)                                        | 247.5 ± 221.4       | 216.4 ± 196.9     | 1.313* | 0.196 |
| Primary diseases                                                 |                    |                  |       |       |
| Chronic glomerulonephritis, n (%)                               | 186 (76.2)          | 91 (74.6)         | 0.120* | 0.730 |
| Diabetic nephropathy, n (%)                                     | 15 (6.2)           | 6 (4.9)           | 0.230* | 0.634 |
| IgA nephropathy, n (%)                                           | 20 (8.2)           | 14 (11.6)         | 1.040* | 0.308 |
| Others, n (%)                                                    | 23 (9.4)           | 11 (9.0)          | 0.02*  | 0.899 |
| First transplantation, n (%)                                    | 244 (100)          | 122 (100)         | NA     |       |
| HLA mismatches                                                  | 2.3 ± 0.83         | 2.3 ± 0.78        | <0.001* | 0.969 |
| Negative PRA, n (%)                                              | 225 (92.2)         | 115 (94.3)        | 0.520* | 0.472 |
| Donors                                                          | n = 182            | n = 122           |        |       |
| Age (year)                                                       | 41.0 ± 13.7         | 40.1 ± 13.5       | 0.595* | 0.762 |
| Gender (male/female), n                                          | 145/37             | 92/30             | 0.770* | 0.380 |
| BMI (kg/m²)                                                     | 21.7 ± 2.9         | 21.9 ± 2.8        | 0.629* | 0.846 |
| Cause of death                                                  |                    |                  |       |       |
| Craniocerebral trauma, n (%)                                    | 113 (62.1)         | 75 (61.5)         | 0.010* | 0.914 |
| Cerebrovascular diseases, n (%)                                  | 45 (24.7)          | 31 (25.4)         | 0.020* | 0.893 |
| Other cause, n (%)                                               | 24 (13.2)           | 16 (13.1)        | 0.000* | 0.986 |
| Hypertension history, n (%)                                      | 31 (17.0)           | 19 (15.6)        | 0.110* | 0.737 |
| Serum creatinine (μmol/L)                                       | 99.8 ± 64.1        | 95.0 ± 60.9       | 0.653* | 0.587 |
| Cold ischemia time (h)                                          | 7.8 ± 4.5          | 7.3 ± 4.1         | 0.984* | 0.326 |
| Warm ischemia time (min)                                        | 9.8 ± 6.5          | 9.4 ± 6.6         | 0.527* | 0.772 |
| Controlled DCD, n (%)                                           | 150 (82.4)         | 104 (85.2)        | 0.430* | 0.514 |
| Uncontrolled DCD, n (%)                                         | 32 (17.6)          | 18 (14.8)         | 0.430* | 0.514 |

Data were presented as mean ± SD or n (%). *Student’s t-test; †Chi-square test; ‡PRA <10% was negative; 10%≤ PRA <30% considered positive; PRA ≥30% excluded from this study. HLA: Human leukocyte antigen; PRA: Panel reactive antibodies; DCD: Donation after cardiac death; BMI: Body mass index; NA: Not available.
duration ≥12 h (OR = 1.342, 95% CI: 1.184–1.521, P = 0.001). Meanwhile, temperature, pump pressure, and left/right kidney were not associated with DGF onset [Table 3]. We used a multivariate logistic regression model that included all the variables that were statistically significantly related with DGF in the univariate analyses to better identify the predictors of DGF. The probability of correlation between the pump pressure and DGF was <0.1 (OR = 1.252, 95% CI: 1.127–1.390, P = 0.087) in the univariate logistic regression models. Therefore, the perfusion pressure was also included in the multivariate analysis of the model. The terminal flow (OR = 0.931, 95% CI: 0.894–0.967, P = 0.011), terminal resistance (OR = 2.190, 95% CI: 1.032–10.20, P = 0.000), and HMP duration (OR = 1.165, 95% CI: 1.008–1.360, P = 0.043) still remained statistically significantly related with DGF after multivariate analysis [Table 3]. According to the results of the univariate and multivariate logistic regression analyses, the terminal flow, terminal resistance, and HMP duration (Referent <12 h) were considered the independent predictors of DGF.

**Hypothermic machine perfusion score development**

The observed overall frequency of DGF posttransplant in the development cohort was 15.6% (n = 38). The methods of Sullivan et al.\(^{23}\) were used to convert the model in Table 3 to a simple point system. Table 3 showed that the risk factors used to develop the scoring model based on whether DGF has occurred, and these variables were selected for the final HMP scoring mode. Table 3 also showed the logistic estimate ORs for all of the HMP variables. The Hosmer-Lemeshow test was 9.15 (P = 0.355) for the HMP risk-scoring mode, indicating that the logistic model was appropriate in the analyses. HMP scores according to the risk model for all predictors are summarized in Table 4. The sum of HMP scores ranged between a minimum of 0 to a maximum of 14 points [Table 4]. The number of recipients at each HMP score level and the corresponding frequency of DGF in the development and the validation cohorts are shown in Table 5. There was a clear increase in the incidence of DGF moving from the low-risk score group to the very high-risk score group. According to the acquired frequencies of DGF associated with different risk scores, we formed four increasingly serious risk categories (scores 0–3, 4–7, 8–11, and 12–14) to increase the number of recipients in each risk category and to heighten the clinical utility of scoring. The incidence of DGF in the four categories of severity in the development cohort set ranged from 4.6% to 66.7% [Table 5].

**Validations of hypothermic machine perfusion score**

The observed overall rate of DGF posttransplant in the validation cohort was 16.4% (n = 20). The incidences of DGF in the validation cohort were close to those in the development cohort in each of the four risk categories [Table 5]. We performed c-statistic analysis of the two datasets to test and compare the diagnostic ability of the HMP scoring mode. The c-statistic of the HMP scores in the validation cohort was 0.706 (95% CI: 0.608–0.811), and it was 0.712 (95% CI: 0.615–0.804) in the development cohort. The c-statistic results were not statistically significantly different [Figure 1]. We also computed for the c-statistics for the terminal flow and the terminal resistance. The c-statistics for the terminal flow and the terminal resistance were 0.503 (95% CI: 0.405–0.613) and 0.597 (95% CI: 0.535–0.672), respectively [Figure 1]. The c-statistic results were statistically significantly less than the HMP scores in the development and the validation cohorts indicating that the HMP score model demonstrated good discriminative power in predicting DGF after kidney transplantation.

### Table 2: HMP variables for transplant kidneys in the development and validation cohorts

| Variables | Development cohorts (n=244) | Validation cohorts (n=122) | t or χ² | P |
|-----------|-----------------------------|---------------------------|---------|---|
| Flow (ml/min) | 93.4 ± 24.1 | 96.9 ± 23.6 | 1.319* | 0.188 |
| Resistance (mmHg·ml⁻¹·min⁻¹) | 0.352 ± 0.140 | 0.359 ± 0.130 | 0.462* | 0.668 |
| Pressure (mmHg) | 32.1 ± 3.0 | 32.1 ± 2.7 | 0.000* | 0.988 |
| Temperature (°C) | 3.95 ± 0.30 | 3.96 ± 0.28 | 0.307* | 0.753 |
| HMP duration (h) | 7.8 ± 2.7 | 7.5 ± 2.4 | 1.039* | 0.280 |
| Left/right kidney, n | 120/124 | 62/60 | 0.090† | 0.768 |

Data were presented as mean ± SD or n (%). *Student’s t-test; †Chi-square test. HMP: Hypothermic machine perfusion.

### Table 3: HMP variables in the univariate and multivariable logistic regression analysis for DGF

| Variables | Univariate analysis | Multivariable analysis |
|-----------|---------------------|------------------------|
| OR        | 95% CI              | P                      | OR        | 95% CI              | P                      |
| Flow (ml/min) | 0.863 | 0.729–0.969 | <0.001 | 0.931 | 0.894–0.967 | 0.011 |
| Resistance (mmHg·ml⁻¹·min⁻¹) | 7.262 | 2.909–15.508 | <0.001 | 2.190 | 1.032–10.20 | 0.000 |
| HMP duration (h)* | 1.342 | 1.184–1.521 | 0.001 | 1.165 | 1.008–1.360 | 0.043 |
| Pressure (mmHg) | 1.252 | 1.127–1.390 | 0.087 | – | – | – |
| Left/right kidney, n | 1.052 | 0.526–2.103 | 0.887 | – | – | – |
| Temperature (°C) | 0.916 | 0.807–1.040 | 0.175 | – | – | – |

*HMP duration referent <12 h. DGF: Delayed graft function; HMP: Hypothermic machine perfusion; OR: Odds ratio; CI: Confidence interval.
**Discussion**

DGF has been recognized as one of the most crucial factors affecting graft function and survival in kidney transplantation.[5,24,25] Donor organ quality is one of the most important factors of DGF. How to evaluate the quality of DCD kidneys has become a critical problem in the kidney transplantation field. Reducing this complication may not only have important clinical significance but may also bring huge economic benefits. HMP has been shown to be superior to static cold storage for kidney preservation[26] due to improved perfusion of the microvasculature, decreased aggregation of blood components, mitigated endothelial activation, and reduced inflammatory up-regulation.[6,7,27]

In the current era of DCD, due to inadequate assessment of donors, many meaningful indicators cannot be collected. Therefore, the quality of the donor kidney cannot be well assessed by donor assessment. HMP solved this problem better; it can better evaluate the quality of kidney from the whole through various parameters. Furthermore, HMP enables the pretransplantation assessment of graft viability and quality and can predict DGF, drawing the attention of the majority of the physicians. It allows the study of perfusion characteristics such as resistance and flow. Current evidence suggests that resistance and flow rate during HMP correlate with kidney-graft function. Resistance at the end of HMP has been shown to be an independent risk factor for the development of DGF.[9,28]

Our data support this connection. In the development cohort, resistance and flow rates were significantly associated with DGF on multivariate analysis. Therefore, parameters of HMP might be a good non-invasive method to replace kidney biopsy for evaluating the quality of DCD kidneys before transplant. A kidney biopsy and histologic scores remain as the gold standard for evaluating quality of kidneys before transplant.[11,12,29]

### Table 4: HMP scoring model in predicting DGF in patients after kidney transplantation

| Variables | Score* |
|-----------|--------|
| Flow      |        |
| >120 ml/min | 0      |
| 100–120 ml/min | 1      |
| 80–119 ml/min | 2      |
| 60–79 ml/min | 3      |
| <60 ml/min | 5      |
| Resistance |        |
| <0.30 mmHg·ml⁻¹·min⁻¹ | 0      |
| 0.30–0.39 mmHg·ml⁻¹·min⁻¹ | 2      |
| 0.40–0.49 mmHg·ml⁻¹·min⁻¹ | 4      |
| 0.50–0.59 mmHg·ml⁻¹·min⁻¹ | 6      |
| ≥0.60 mmHg·ml⁻¹·min⁻¹ | 8      |
| HMP time  |        |
| <12 h     | 0      |
| ≥12 h     | 1      |

*The risk score was derived from a competing risk model with DGF. To calculate the risk score, points for all factors are summed up. DGF: Delayed graft function; HMP: Hypothermic machine perfusion.

### Table 5: Predicted risk and risk categories of DGF in patients after kidney transplantation based on the HMP scoring model

| Characteristics | Development cohorts | Validation cohorts |
|-----------------|---------------------|--------------------|
| HMP score       | Total, N | DGF, n | Incidence (%) | Total, N | DGF, n | Incidence (%) |
| 0               | 21       | 1      | 4.8           | 8        | 0      | 0           |
| 1               | 20       | 1      | 5.0           | 20       | 1      | 5.0         |
| 2               | 48       | 2      | 4.2           | 16       | 1      | 6.3         |
| 3               | 20       | 1      | 5.0           | 14       | 1      | 7.1         |
| 4               | 25       | 2      | 8.0           | 16       | 2      | 12.5        |
| 5               | 20       | 2      | 10.0          | 14       | 2      | 14.3        |
| 6               | 20       | 3      | 15.0          | 6        | 1      | 16.7        |
| 7               | 16       | 3      | 18.8          | 6        | 1      | 16.7        |
| 8               | 9        | 2      | 22.2          | 4        | 1      | 25.0        |
| 9               | 10       | 3      | 30.0          | 5        | 2      | 40.0        |
| 10              | 9        | 3      | 33.3          | 2        | 1      | 50.0        |
| 11              | 8        | 3      | 37.5          | 2        | 1      | 50.0        |
| 12              | 6        | 3      | 50.0          | 5        | 3      | 60.0        |
| 13              | 9        | 6      | 66.7          | 3        | 2      | 66.7        |
| 14              | 3        | 3      | 100.0         | 1        | 1      | 100.0       |
| Risk categories |         |        |               |         |        |             |
| Low (0–3)       | 89       | 5      | 4.6           | 58       | 3      | 5.2         |
| Moderate (4–7)  | 81       | 10     | 12.3          | 42       | 6      | 14.3        |
| High (8–11)     | 36       | 11     | 30.6          | 13       | 5      | 38.5        |
| Very high (12–14) | 18     | 12     | 66.7          | 9        | 6      | 66.7        |
| Overall         | 244      | 38     | 15.6          | 122      | 20     | 16.4        |

DGF: Delayed graft function; HMP: Hypothermic machine perfusion.
is a time-consuming and invasive process that requires experienced pathologists to assess kidney quality. We have established an HMP scoring model to identify DGF at a high as well as a low-risk pretransplantation score group. Furthermore, we validated the HMP scoring model that was similar to that of the development cohort (0.706 vs. 0.712), suggesting high stability of the HMP predictive score model. We also conducted a sensitivity analysis to assess the ability of a single HMP variable to identify DGF. The final risk model had a higher c-statistic score in the development and validated cohorts as compared to the single HMP variables such as terminal resistance and flow rate. This indicates that using the HMP scoring model is superior as compared to using a single HMP parameter in evaluating DCD kidney quality and predicting DGF.

The present study derived and validated a potential clinical prediction tool rather than a decision rule. It is to aid the attending physician who will make the clinical decision. For instance, based on the low- and moderate-risk categories, we recommend that the DCD kidney can be used with minimal risk of DGF. However, at high-risk categories, we recommend being cautious in the application of the DCD kidney and should be used in specific clinical situations.

In summary, our findings suggest that the HMP scoring model may be a good noninvasive tool for evaluating the quality of DCD kidneys, and it is potentially useful for physicians in making optimal decisions regarding donor organ offers.

**Financial support and sponsorship**
This work was supported by grants from the Fundamental Research Funds for the Central Universities (No. xjj2018091), Major Clinical Research Projects of the First Affiliated Hospital of Xi’an Jiaotong University (No. XJUTU1AF-CRF-2015-005), Scientific and Technological Breakthrough in Social Development of Shaanxi Province (No. 2016SF-246), and the National Natural Science Foundation of China (No. 81670681 and 81760137).

**Conflicts of interest**
There are no conflicts of interest.
Pulsatile perfusion reduces the incidence of delayed graft function. Transplant Direct 2017;3:e155. doi: 10.1097/01.TXD.0000000000000672.

Gill JG, Kong J, Eng M, Landaus B, Gill JS. Pulsatile perfusion reduces the risk of delayed graft function in deceased donor kidney transplants, irrespective of donor type and cold ischemic time. Transplantation 2014;97:668-74. doi: 10.1097/TP.0000000000000214.

Yochmans I, O’Callaghan JM, Pirenne J, Ploeg RJ. Hypothermic machine perfusion of kidneys retrieved from standard and high-risk deceased donors. Am J Transplant 2016;16:1526-39. doi: 10.1111/ajt.13655.

Heilmann RL, Mathur A, Smith ML, Kaplan B, Reddy KS. Increasing the use of kidneys from unconventional and high-risk deceased donors. Am J Transplant 2016;16:3086-92. doi: 10.1111/ajt.13867.

Sung RS, Christensen LE, Leichtman AB, Greenstein SM, Distant DA, Wynn JJ, et al. Determinants of discard of expanded criteria donor kidneys: Impact of biopsy and machine perfusion. Am J Transplant 2008;8:783-92. doi: 10.1111/j.1600-6143.2008.02157.x.

Hanley JA, McNeil BJ. The meaning and use of the area under the receiver operating characteristic (ROC) curve. Radiology 1982;143:29-36. doi: 10.1148/radiology.143.1.7063747.

Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29-36. doi: 10.1148/radiology.143.1.7063747.

Application of machine perfusion preservation as a viability test for marginal kidney graft. Transplantation 2006;82:1425-8. doi: 10.1097/01.MOT.0000243733.77706.99.

van Smaalen TC, Hoogland ER, van Heurn LW. Machine perfusion viability testing. Curr Opin Organ Transplant 2013;18:168-73. doi: 10.1097/MOT.0b013e32835fb1b.

Henley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29-36. doi: 10.1148/radiology.143.1.7063747.

Vanlaargadda SG, Coca SG, Formica RN Jr, Poggio ED, Parikh CR. Association between delayed graft function and allograft and patient survival: A systematic review and meta-analysis. Nephrol Dial Transplant 2009;24:1309-47. doi: 10.1093/ndt/gfn667.

Jochmans I, Moers C, Smits JM, Leuveninck HG, Treckmann J, Paul A, et al. The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 2011;11:2214-20. doi: 10.1111/j.1600-6143.2011.03685.x.

Jochmans I, Moers C, Smits JM, Leuveninck HG, Treckmann J, Paul A, et al. The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 2011;11:2214-20. doi: 10.1111/j.1600-6143.2011.03685.x.

Jochmans I, Moers C, Smits JM, Leuveninck HG, Treckmann J, Paul A, et al. The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 2011;11:2214-20. doi: 10.1111/j.1600-6143.2011.03685.x.

Jochmans I, Moers C, Smits JM, Leuveninck HG, Treckmann J, Paul A, et al. The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 2011;11:2214-20. doi: 10.1111/j.1600-6143.2011.03685.x.

Jochmans I, Moers C, Smits JM, Leuveninck HG, Treckmann J, Paul A, et al. The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 2011;11:2214-20. doi: 10.1111/j.1600-6143.2011.03685.x.
基于低温机械灌注变量预测移植肾功能延迟恢复的评分模型构建

摘要

背景：低温机械灌注（Hypothermic machine perfusion, HMP）在心脏死亡移植中应用越来越广泛，但对其在供肾质量评估和移植延迟功能（delayed graft function, DGF）预测仍存在争议。因此，我们应用HMP参数设计评分模型，以期识别DGF的最高风险，并为器官分配和DCD肾脏评估提供指导和建议。

方法：从2012年9月1日到2016年8月31日，将366个符合研究标准的肾脏按照2:1随机分成开发组和验证组。开发组的HMP变量作为预测DGF的候选因子。采用多元Logistic回归分析确定DGF的独立预测因子（P<0.05）。根据概率比（ORs）值，给每个HMP变量分配一个整数加权，变量的整数加权总和代表每个肾脏的DGF风险评分。验证组数据用于验证评分模型的准确性和可靠性。

结果：HMP持续时间（OR = 1.165, 95%CI: 1.008-1.360, P = 0.043），阻力指数（OR = 2.190, 95%CI: 1.032-10.20, P = 0.000），灌注流量（OR = 0.931, 95%CI: 0.894-0.967, P = 0.011）是DGF的独立预测因子。HMP预测评分范围为0～14分，从低风险评分到高风险评分，DGF的发生率升高。根据DGF不同风险评分的频率，我们分为4个风险类别（0-3、4-7、8-11和12-14）。HMP评分模型在验证组中也具有良好的预测能力，c统计量为0.706，对DGF的预测能力明显优于灌注流量（P = 0.012）和阻力指数（P = 0.006）。

结论：HMP评分模型是评价DCD肾脏质量、预测DGF的无创性工具，对器官移植医生客观选择DCD供肾、指导DCD供肾的分配具有潜在的应用价值。