Cox Regression Model Analysis of Infection in Renal Transplants After Operation

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ABSTRACT

Background. The objective of this study was to explore the factors that affect infections after renal transplant, establishing the Cox model to forecast infection for patients of renal transplant.

Methods. Data were collected from patients who had renal transplantation in Nanking Jinlin Hospital from January 2011 to April 2015 (n = 305 transplants). There were 296 individual data that could be used after deleting the people who were lacking some data, changing the main immunosuppressants during the first year, losing follow-up, and data writing that was not fully 1 year after the operation; 296 individuals were divided by 3:7. The 206 data of patients (7/10 of the total individuals) were used to analyze and build a model, and the rest of the data were used to verify the model, analyzing the 206 data with Cox regression, discovering the factors that affect the infection after renal transplant independently, building the model, and verification.

Results. Cox regression showed that there are three independent factors that affect infections after renal transplant: X3, the donor type (relative risk [RR] = 1.929, $P = .037$); X9, dialysis time (RR = 1.017, $P = .032$); and X13, human leukocyte antigen (HLA) match (RR = 0.257, $P = .013$). The model is: PI = 0.657X3 + 0.017X9 − 1.359X13. All PI for the 206 individuals were calculated and then divided into three groups: the low-risk group, the median-risk group, and the high-risk group. The model was verified by calculating the PI for all 90 people. The log-rank test showed that the survival rates among these groups were significantly different ($P < .001$).

Conclusions. Donor type, dialysis time, and HLA match are all factors that affect infection after renal transplant. Donor type and dialysis time were the dangerous factors for infection, but HLA match was the protecting factor. The model depends on these three factors and could forecast infection after renal transplant.

WITH the development of kidney transplantation, an increasing number of people who have end-stage renal disease hope to get a safe and effective therapy to prolong life. Since 1954, when the first kidney transplantation was performed, the skill of operation and drug therapy were enhanced so that the survival rates of transplanted kidney are increasing. However, the postoperative complications cannot be avoided absolutely, such as rejection and infection, decreasing life quality, and rising burden of physiology and money paying for patients. Some researchers believe that bacterial infection after renal transplantation extends the hospital stay, decreasing creatinine clearance rate for transplants and increasing the risk of operation once more [1]. Furthermore, infection is the main reason for death after renal transplantation within 1 year [2]. There are many possible relevant factors that could affect infection after operation. Thus, the

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Table 1. Characteristics of the Basic Data of 206 Renal Transplant Patients

Characteristics	Value
Recipient age, years	35.59 ± 10.66
Male sex	137
Donor type	
Relative living	83
Cadaveric deceased donor	123
Hypertension	188
Diabetes	15
Immunosuppression choice	
TAC	175
TAC trough blood concentration (ng/mL)	6.85 ± 1.8
CsA	31
CsA trough blood concentration (ng/mL)	217.69 ± 1.32
Steroid pulse therapy	27
Dialysis	164
Dialysis time (months)	11.78 ± 13.25
HLA match	
0–4	178
5–8	28

forecast of infection after kidney transplantation rationally is necessary and significant. In our research, we considered the baseline data first, such as sex, age, hypertension or not, and diabetes or not, which could have the possibility of infection. Furthermore, usage of immunosuppressants was considered in the study. Although different immunosuppressants have different mechanisms, they act on T- and B-lymphocytes, decreasing the immune function and increasing the risk for infection. At the same time, the donor type, human leukocyte antigen (HLA) mismatch, dialysis or not, and the time of dialysis are all included. We used Cox regression and the Cox proportional hazard model to do the research. This method is used for analysis of factors that could affect prognosis of disease or tumor, in the narrow sense. However, it is suitable to analyze all events that have the end point, taking advantage of incomplete data and information to find the independent effective factors and the relative risk, respectively, and then a making model to predict and evaluate the risk of similar events. Therefore, it is reasonable to use this method to forecast the risk of infection for patients after renal transplantation so that the personalized immunosuppressive and antibiotic treatment could be implemented effectively.

METHODS

Study Population

For this research, we considered the data of renal transplants from January 2011 to April 2015 in JinLin Hospital (n = 305). After deleting the individuals who lacked clinical data, changed the main immunosuppressive in 1 year, and data writing not full at 1 year (n = 9), we had the total number of 296 people who could be observed.

End Point and Data Dividing

We defined infection as the end point. The infection end point is the first-time infection event after kidney transplantation within 1 year, which included all of the severe or slight infections.

The 296 individuals were divided randomly into two groups at the rate of 7:3. The first group's (n = 206) data were used for analyzing and modeling; the second group's (n = 90) data were used for validation.

HLA match analyzed the matching number of HLA between the recipients and donors (HLA-A, HLA-B, HLA-DQ, HLA-DR).

Criteria for Infections

Pulmonary infection criteria included (a) fever; (b) cough and expectoration recently or if these events become worse; (c)rales; (d) white blood cell (WBC) count $>10 \times 10^9$/L or $<4 \times 10^9$/L; and (e) radiography or CT shows shadow of flake. Any of a, b, c, or d plus e could ensure pulmonary infection if patients do not have other lung disease.

Diagnostic criteria for intestinal infection were fever (≥38°C), nausea, vomiting, or diarrhea 3 times or more in 1 day, except for chronic enteritis or any other non-infection disease. Flora imbalance was found in examined stools.

Diagnostic criteria for urinary tract infection were the presence of urinary symptoms suggesting infection; the presence of indicators of urinary tract invasion by microorganisms (pyuria, hematuria, or immune response); and the presence of bacteriuria on urine cultures [3].

Diagnostic criteria for urinary tract infection were fever (core temperature >38.3°C); heart rate >90 bpm or >2 standard deviations (SD) above the normal value for age; tachypnea >30 bpm; altered mental status; and significant edema or positive fluid balance (>20 mL/kg over 24 hours).

Inflammatory Parameters

Inflammatory parameters included leukocytosis (WBC count >12,000/μL); leukopenia (WBC count <4000/μL); normal WBC count with >10% immature forms; plasma C-reactive protein >2 SD above the normal value; and plasma procalcitonin >2 SD above the normal value [4].

Statistical Analyses

Data were input into EXCEL 2013 and analyzed with the use of IBM SPSS 19. The Cox proportional hazard regression model was used to analyze the 13 factors that possibly affect infections after

Table 2. Evaluation of Factors Relevant to Infection After Renal Transplant

No.	Variable	Value
X1	Recipient age	Real age
X2	Sex	Male = 1, female = 0
X3	Donor type	Relative living = 0, cadaveric = 1
X4	Hypertension	Yes = 1, no = 0
X5	Diabetes	Yes = 1, no = 0
X6	Immunosuppression	TAC + MMF + prednisone = 1, CsA + MMF + prednisone = 2
X7	Donor age	Real age
X8	Dialysis	Yes = 1, no = 0
X9	Dialysis time	Real time (months)
X10	Blood concentration	Real number (ng/mL)
X11	Dosage MMF	Real number (mg/bid)
X12	Steroid pulse therapy	Yes = 1, no = 0
X13	HLA match	From 0 to 4 match = 1, from 5 to 8 match = 2