Available online at www.sciencedirect.com
ScienceDirect
Transplantation Reviews 22 (2008) 21–26
TRANSPLANTATION Reviews
www.elsevier.com/locate/trre

Predicting delayed graft function and mortality in kidney transplantation

Domingo Hernández[a,*], Margarita Rufino[a], José Manuel González-Posada[a], Sara Estupiñán[a], Germán Pérez[a], Domingo Marrero-Miranda[a], Armando Torres[a], Julio Pascual[b]

[a]*Department of Nephrology, Hospital Universitario de Canarias, Ofra s/n, 38320 La Laguna, Tenerife, Spain*
[b]*Department of Nephrology, Hospital Ramón y Cajal, 280034 Madrid, Spain*

Abstract

Kidney transplantation (KT) is the treatment of choice for end-stage renal failure, but such patients are increasingly older and have additional comorbid conditions leading to high mortality rates after transplantation. Delayed graft function is a common complication after KT, especially in recipients who receive expanded criteria donor, and these complications are associated with a poorer graft survival in the long term. Taken together, an appropriate assessment of comorbidity grouped in prognostic indexes could be a useful tool to make crucial therapeutic decisions at the time of transplant. Allocation systems based upon a recipient risk score, as well as identification of risk factors for delayed graft function, may improve outcomes after KT. The aim of this review is to assess the contribution and utility of comorbid conditions, grouped in prognostic indexes to predict and improve kidney transplant outcomes.

1. Introduction

Kidney transplantation (KT) is the treatment of choice for end-stage renal failure, but such patients are increasingly older and have additional comorbid conditions leading to high mortality rates after transplantation. Indeed, there is agreement that this poor prognosis is due to an interaction between high prevalence of classic risk factors and inherent conditions to KT [1]. Hence, cardiovascular death rate is higher than in the general population, even after stratifying for age, sex, and race. Moreover, comorbidity needs to be adjusted in multiple clinical researching to assess the impact of long-term transplantation on patients' outcomes. Despite these facts, the relative performance of various comorbidity indexes (CIs) in predicting outcome in this population is not well known.

Delayed graft function (DGF), defined as the need for dialysis within 1 week after KT, is strongly affected by the quality of the deceased donor kidney. The presence of DGF is an independent risk factor for both acute rejection and impaired renal function at 1 year after KT. Moreover, DGF is associated with decreased long-term graft survival. For these reasons, a prognostic index for assessing the risk for DGF may be a very useful tool to improve outcomes in the short and long term after KT.

The aim of this review is to assess the contribution of kidney transplant recipient comorbid conditions grouped in prognostic indexes on kidney transplant outcomes. We will focus on (*a*) utility of a mathematical nomogram to predict DGF in kidney transplant recipients and (*b*) prognostic indexes for mortality after KT.

2. Predicting DGF in kidney transplant recipients

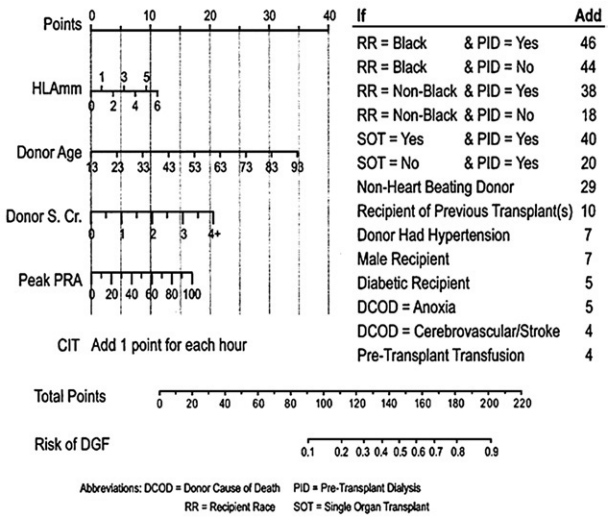
Delayed graft function is a frequent complication after KT (20%–30%) and is defined as the need for dialysis in the first week after transplantation. Although the mechanisms involved in its pathogenesis are not well understood, the detrimental effect of DGF on transplant outcomes is well documented [2,3]. Delayed graft function may contribute to graft loss and may predispose to acute rejection. Ischemia/reperfusion injury of an allograft lead to immunologic events such as leukocyte adherence, inflammation, and tissue damage that can up-regulate immune response, increasing organ alloreactivity [4]. Moreover, expanding the donor pool by using marginal donors has been adopted at most transplant centers, and this strategy makes up a great risk for DGF, primary nonfunction, and shortened graft survival. In addition, DGF has a considerable economic cost that is the

* Corresponding author. Tel.: +34 922678545; fax: +34 922678545.
E-mail address: domingohernandez@gmail.com (D. Hernández).

0955-470X/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.trre.2007.09.007

result of prolonged patient hospitalization and the increased cost of patient management (graft biopsies, immunosuppressive drug monitoring, dialysis, etc). Thus, interventions that reduce the incidence of DGF or prevent development of DGF are needed to save costs and improve the outcome after KT in the modern transplant era.

Irish et al [5] developed an index, or nomogram, that quantifies the likelihood of DGF after KT by using donor and recipient potential risk factors before transplantation. They used data available from 13 846 adult cadaveric renal transplant recipients recorded in the United States Renal Data System. Graft losses within the first 24 hours after surgery were excluded from analysis as well as patients whose DGF information was missing or unknown. By means of a multivariable logistic regression analysis, factors contributing to DGF were identified. There were 16 donor or recipient variables significantly associated with DGF, although the most significant were a history of pretransplantation dialysis followed by use of a non–heart-beating donor and recipient of a single organ transplant. The predictive accuracy of the model was assessed by a concordance c index. In addition, the predictive accuracy of the model was graphically displayed by receiver operating characteristic (ROC) curve, whereby the c index is identical to the area under the ROC curve. After validating the logistic regression model, the 16 donor or recipient variables were used to create a functional nomogram as a tool for identifying patients at risk for developing DGF. Specific points relative to the effect on DGF were assigned to the 11 categorical variables, and a point scale was used to assign points to the 5 continuous variables (Fig. 1). A point score of approximately 120 correlates with the current mean rate of DGF. Likewise, a point score of 145 predicts a 50% chance of DGF. This nomogram can be used to determine optimal allograft strategies and direct interventions to prevent or minimize DGF. However, notable risk factors that may affect the incidence of DGF, such as body mass index, type of dialysis, or expanded criteria characteristics of the donors, were excluded. In addition, this model was estimated using data from the late 1990s, and the risk of DGF has changed over time.



If		Add
RR = Black	& PID = Yes	46
RR = Black	& PID = No	44
RR = Non-Black	& PID = Yes	38
RR = Non-Black	& PID = No	18
SOT = Yes	& PID = Yes	40
SOT = No	& PID = Yes	20
Non-Heart Beating Donor		29
Recipient of Previous Transplant(s)		10
Donor Had Hypertension		7
Male Recipient		7
Diabetic Recipient		5
DCOD = Anoxia		5
DCOD = Cerebrovascular/Stroke		4
Pre-Transplant Transfusion		4

Fig. 1. Nomogram for predicting the risk of DGF in deceased kidney transplant recipients [5]. HLAmm indicates HLA mismatch; S.Cr, serum creatinine; PRA, panel-reactive antibody; CIT, cold ischemia time; RR, recipient race; PID, pretransplantation dialysis; SOT, single organ transplant; DCOD, donor cause of death. Reprinted with permission from Irish et al [5].

Recently, the validity of the Irish nomogram in the United States was questioned by other authors using all deceased renal transplants performed at a single center [6]. There was overlapping in nomogram score values between patients with and without DGF. In particular, the mean nomogram DGF risk was 0.45 ± 0.14 (95% confidence interval, 0.40–0.49) for the 42 DGF-positive patients and 0.40 ± 0.14 (95% confidence interval, 0.38–0.43) for the DGF-negative subjects ($P = .07$). The calculated risk of DGF ranged from 10% to 78% for recipients with DGF and 10% to 83% for those without DGF. However, the sample size was too small in the study of Grossberg et al [6], and these authors used the mean and median risk scores to evaluate the nomogram. These statistical tests cannot be used to validate a predictive model. Therefore, there exists controversy about prospective application of this nomogram on a case-by-case basis as a reliable tool for making treatment decisions at the bedside after KT, focused at ameliorating DGF.

Neural networks may be useful tools in predicting overall clinical outcomes such as DGF. In particular, artificial neural networks are an extension of traditional statistical techniques and may offer a more flexible modeling environment than any of the traditional approaches, including other statistical methods [7,8]. In addition, they are most closely related to regression models such as logistic regression for prediction and discriminant analysis for classification. The dependent variable DGF is predicted as a nonlinear function of a linear combination of the product of the independent variables and the neural network parameters. However, an artificial neural network cannot identify individual risk factors for a given clinical event such as DGF. In a retrospective cohort study performed in 304 kidney transplant recipients who received prednisone, cysclosporine, and azathioprine for induction, predictions for DGF from the neural network were compared with a standard technique of logistic regression, which allows us to evaluate specific risk factors for DGF [9]. Logistic regression analysis was more sensitive to prediction of no DGF (91% vs 70%), whereas the neural network was more sensitive to prediction of yes for DGF (56% vs 37%). Moreover, overall prediction accuracy for logistic regression and the neural network was 64% and 63%, respectively. Logistic regression was 36.5% sensitive and 90.7% specific, whereas the neural network was 63.5% sensitive and 64.8% specific. These findings indicate that the use of computers to predict DGF may be useful in guiding the selective use of immunosuppressants to minimize these complications, especially in high-risk patients.

Finally, changes in urine concentrations of biomarkers such as urine neutrophil gelatinase–associated lipocalin (NGAL) and interleukin 18 (IL-18) have been used as an index of DGF after renal transplantation. Both urine NGAL and IL-18 have been significantly higher since day 0 posttransplant in patients with DGF compared with recipients of living-donor and deceased-donor kidney without DGF. In addition, the ROC curve for prediction of DGF based on urine NGAL or IL-18 at day 0 showed an area under the curve of 0.9 for both biomarkers. By multivariate analysis, both urine biomarkers were able to predict the trend in serum creatinine in the posttransplant period after adjusting for other confounder variables [10]. Other serum biomarkers such as plasma concentrations of hypoxanthine and xanthine have also been used as predictors of DGF [11], but future studies are needed to confirm these findings.

In summary, comorbidities grouped in CI and scoring systems based on recipient risk factors and deceased donor characteristics may allow us appropriate allocation systems and to identify high-risk patients to make crucial therapeutic decisions at the time of transplant for improving outcome after KT.

3. Predicting mortality after KT

The construct *comorbidity* reflects the aggregate effect of all clinical conditions that a patient may have, excluding the disease of primary interest. Because there is no gold standard, researchers validate measures of comorbidity by how well they predict worse outcomes, more health care use, and increased heath care expenditures. For these reasons and given the difficulties measuring comorbidity, an appropriate assessment of comorbidity could be CIs [12,13]. They intend to collect the cumulative impact of multiple comorbid diseases to predict survival. Moreover, single scores for summarizing comorbidity are of particular interest to researchers who use large databases because the first stage of such studies is to leak information into an intelligible and manageable set of proxy variables. In this process, the benefits of simplification usually seem much greater than the risks of oversimplification.

Several such CIs have been validated in uremic patients, and each index has been accurately shown to predict mortality among a dialysis population. Indeed, based on age and number of comorbid conditions, these patients have been successfully classified to have low, medium, or high risk of death [14-17]. However, the application of CIs in KT has not been widely studied. A prognostic index that estimates long-term mortality in these patients may be a useful tool in identifying groups at high risk for poor outcomes in whom early targeted treatment interventions may be indicated and, consequently, help minimize mortality. In addition, prognostic indexes are also essential for comparing outcomes among different clinical studies and populations, including kidney transplant recipients. Finally, they provide an objective means to characterize case mix, which may help to administer more reasonably the health resources.

The usefulness of a CI lies in its relative objectivity in assessing the risk of mortality in any given patient. In general, the predictive performance of comorbidity scores derived from databases depends on several factors, including (1) the clinical conditions included in a score and their relative weights, (2) the distribution of comorbid conditions in the source population, (3) the end point of a study, and (4) the accuracy of the data [18,19]. To assess the data quality, information should be obtained from medical records with great precision to identify implausible values. Moreover, missing data must be recognized and introduced in the final analysis. Accordingly, we developed and validated, for the first time, a new prognostic index that met these criteria in 1293 kidney transplant recipients who were randomly assigned to 2 groups: a modeling population (n = 646), used to generate the new index, and a testing population (n = 647), used to test this new index, so that every patient in the database had an equal probability of being included in the modeling or testing population [20]. Thus, this testing group was used to validate the new index. We estimated the predicted risk of death for each subject on the basis of a multivariable Cox model in the modeling population. The largest weights (β coefficient) were obtained for being older than 60 years, impaired renal function at discharge, and pretransplant cardiovascular disease, followed by left ventricular hypertrophy, diabetes, vascular calcifications, time on dialysis of more than 48 months, and acute tubular necrosis. We calculated a score based on the sum of the respective weights and allocated patients into tertiles of risk (low, medium, and high). Resembling the clinical practice in KT, we elaborated a risk index combining peritransplant risk factors for mortality in the final model using a simple 8-point checklist: age, pretransplant cardiovascular disease, renal dysfunction at discharge, cardiac hypertrophy, vascular calcification, diabetes, time on dialysis, and acute tubular necrosis (Table 1). As a result, our new index accurately predicted the risk of death in this population. Overall lower survival rates were observed with increasing risk classes in the testing population (log-rank test = 18, $P = .0001$; Fig. 2). The 8-year survival rate ranged from 96% in the lowest-risk tertile to 64% in the highest-risk tertile in the modeling population and from 89% to 64% in the testing group. The discrimination of the final model for overall score was better in the modeling population (ROC area = 0.69) than in the testing group (ROC area = 0.65). Finally, univariate Cox regression in the testing population showed that mortality risk significantly increased with increasing risk classes (medium risk: relative risk = 3.8, 95% confidence interval = 1.5–9.5, $P = .004$; high risk: relative risk = 6.3, 95% confidence interval = 2.4–16.2, $P = .0001$). The predictive power of this new index is likely related to the inclusion of multiple comorbidity and variables specific to the transplant population. Although important risk factors of comorbidity,

Table 1
Stratification of mortality for kidney transplant recipients according to the Hernandez et al [20] CI

Risk group	Inclusion criteria
Low	Age <50 yr and no comorbid illness *
Medium	Age 50–60 yr or Age <50 yr with pretransplant cardiovascular disease † or impairment of renal function at discharge (SCr >2.5 mg/dL) or Age <60 yr with any one of the following: LVH, diabetes, vascular calcifications, time on dialysis >48 mo, or acute tubular necrosis
High	Age >60 yr or Age 50–60 yr with pretransplant cardiovascular disease † or impairment of renal function at discharge (SCr >2.5 mg/dL) or Any age with pretransplant cardiovascular disease † or impairment of renal function at discharge (SCr >2.5 mg/dL) and any one of the following: diabetes, vascular calcification, LVH, or time on dialysis >48 mo or Any age with pretransplant cardiovascular disease † and impairment of renal function at discharge (SCr >2.5 mg/dL)

The sum of each β-coefficient (multivariate Cox analysis) in medium- and high-risk groups ranged from 0.57 to 1.38 and from 1.39 to 3.12, respectively.
LVH, left ventricular hypertrophy; SCr, serum creatinine.
Reprinted with permission from Hernandez et al [20].

* No comorbid illness includes absence of diabetes, pretransplant cardiovascular disease, LVH, vascular calcifications, impairment of renal function at discharge, acute tubular necrosis, and time on dialysis more than 48 months.

† Pretransplant cardiovascular disease includes ischemic heart diseases, stroke, and peripheral artery disease.

such as immunosupressants, metabolic disorders, or infections, emerging during follow-up were not recorded, this simple prognostic index applicable at the bedside may accurately predict survival in kidney transplant recipients after discharge. In addition, this may facilitate decisions on the most appropriate therapeutic measures for minimizing mortality, especially in high-risk groups.

A more recent study using data from the Canadian Organ Replacement Registry tested the ability of 4 CIs (the Charlson comorbidity index [CCI], the Index of Coexistent Diseases, the Davies index and the Khan scoring system) to predict mortality by using a Cox regression model [21]. The CCI is the most commonly used and most validated index for both peritoneal dialysis and hemodialysis population [15-17,22-24]. This index uses a simple weighted scoring system based on the presence or absence of each of 19 variables (Table 2) [22]. Given that one of the variables is the presence or absence of moderate to severe renal disease, the minimum score for all patients with end-stage renal disease is 2. The Index of Coexistent Diseases scores both severity and type of comorbidity [17]. The final score normally is summarized as 1 of 4 categories (normal, mild, moderate, and severe) but can be reported as a detailed description of

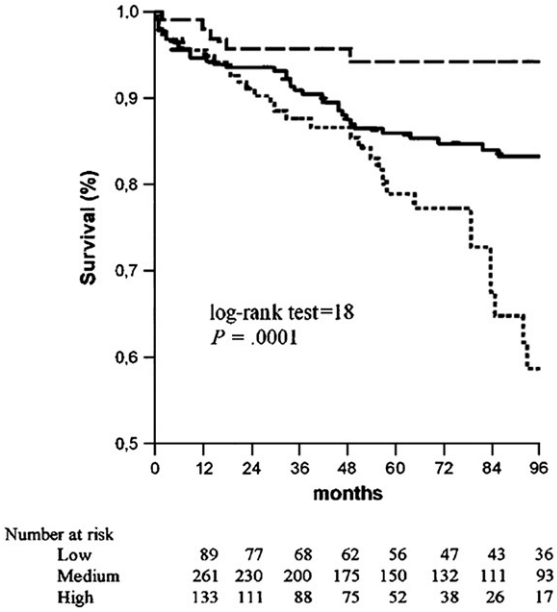


Fig. 2. Kaplan-Meier curves for the Hernandez et al [20] index according to risk groups in the testing population (n = 647; log-rank analysis, $P = .0001$). Broken line indicates low risk; solid line, medium risk; dotted line, high risk. Reprinted with permission from Hernandez et al [20].

comorbidity. The Davies index uses the nonweighted sum of 7 variables to determine comorbidity risk [25]. It reports results as 3 distinct risk groups (mild, moderate, and severe). The Khan scoring system uses a combination of age cutoff values with selected comorbid conditions [15]. This score also is reported as 3 different categories of risk. For each

Table 2
Assigned weights of comorbidity according to the Charlson comorbidity index

Assigned weights	Conditions
1	Myocardial infarction
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Peptic ulcer
	Connective tissue disease
	Mild liver disease
	Diabetes
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end-organ damage
	Tumor
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	AIDS

Reprinted from Journal of Chronic Diseases, Vol 40, Charleson ME et al, A new method of classifying prognostic cormorbidity in logitudinal studies: development and validation, 11, 1987, with permission from Elsevier.

individual, comorbidity was scored by using (1) individual disease indicators, (2) a single summary score equal to the total number of comorbid conditions, and (3) the CIs mentioned. Table 3 shows methods used to convert registered comorbidity data into CIs. The various scores were introduced into the regression models. The best comorbidity score was judged to be the score for the model with the highest likelihood ratio statistic. Model covariates included donor source, age, race, sex, treatment period, primary renal disease cause, months on dialysis, and comorbidities. From a total of 6324 patients included, 22% had at least 1 comorbid condition at baseline, but a large of proportion of patients (71%) had no comorbid conditions at the time of registration. After adjustment for age, sex, and the cause of renal disease, increased comorbidity was associated with reduced patient survival. Of all CIs tested, the model containing the CCI offered the best fit achieving the highest likelihood ratio statistic. In addition, the model containing log-CCI had an index of concordance of 74%. Thus, this index may be a useful tool for the measurement of comorbidity in kidney transplant recipients. Hence, this same group elaborated charts of survival based on comorbid condition in these patients [26]. However, multiple risk factors inherent to the peritransplant process, such as acute rejection, acute tubular necrosis, and immunosuppressants, among others, were not included in the model. Thus, the relative impact of each of these conditions on survival could be omitted. In addition, the application of this CI is time consuming, which may limit its utility and diffusion in the field of renal transplantation.

Later, the CCI was used to assess the comorbidity conditions in 715 patients who underwent KT in a single center [27]. The impact of pretransplantation comorbidity on the development of acute cellular rejection after transplantation and patient and graft survival was examined. The most common comorbid conditions found in the population of this study were diabetes (30%) and heart failure (12%). Unadjusted graft survival and patient survival were significantly decreased in patients with higher comorbidity (CCI score, ≥5). In multivariate-adjusted models, high comorbidity (CCI score, ≥5) was associated with an increased risk for patient death, both in the perioperative period (hazard ratio, 3.2; 95% confidence interval, 1.32–7.78 $P = .01$) and after first 3 months of KT (hazard ratio,

Table 3
Comorbidity scoring method used by Jassal et al

Comorbid Conditions	CORR Database Entry and Comments About Interpretation	CCI Score (original)	CCI Scoring Used	Hemmelgam CCI Scoring Used	Davies Score
Angina	Y/N	0	0	0	
Previous myocardial infarct	Y/N	1	1	2	
Coronary artery bypass surgery	Y/N	0	0	0	
Pulmonary edema/congestive cardiac failure	Y/N	1	1	2	1
Diabetes or diabetes with end-organ disease	Y/N; details if type 1 or 2 only	1	2*	2	1
	Assumed to be diabetes with end-organ disease	2			
Cerebrovascular accident	Y/N				
With residual deficit	No details of deficit recorded	2	2*	2	0
Without residual deficit	Therefore assumed to have deficit	1			
Peripheral vascular disease	Y/N	1	1	1	1
Dementia	Not recorded	1	(1)†	(1)†	0†
Chronic obstructive lung disease	Y/N	1	1	1	0
Connective tissue disease	Recorded under other serious illness and/or as primary renal cause	1	1	1	1
Ulcer disease	Not recorded in registry	1	(1)	d)	0
Mild liver disease	Recorded under other serious illness	1	1	0	0
Moderate or severe renal disease	Assumed to be-present in all patients	2	2	2	0
Any tumor or leukemia or lymphoma or metastatic solid tumor	Only recorded as malignancy Y/N	2	2†	2†	2†
		6†			
Moderate or severe liver disease	Recorded under other serious illness	3	3†	2†	0†
Acquired immunodeficiency syndrome	Recorded under other serious illness	6	6	0	0
Other serious disease	Y/N with text description	NA	NA	NA	1‡

NOTE. Parentheses denote the score that is appropriate for the comorbid condition; however, data about presence or absence were not available on the registry database. Y/N indicates the comorbid condition is recorded as a unique variable as being present or absent.
Abbreviation: NA, not applicable.
Reprinted with permission from Jassal et al [21]. This article was published in Am J Kidney Dis, Vol 46, Jassal et al, Baseline cormorbidity in kidney transplant recipients: a comparison of cormorbidity indices, 136−42, Copyright Elsevier, 2005.

* A higher score was assumed for all patients because detailed information was not available through the registry.
† Comorbid conditions believed to be unlikely in transplant candidates.
‡ Using the Davies score, 1 point is given if there is any other serious illness(es); eg, chronic obstructive lung disease, cirrhosis, or psychotic illness.

2.63; 95% confidence interval, 1.62–4.28; $P < .001$). A CCI score of at least 5 was also associated with graft failure, although the adjusted risk did not reach statistical significance (hazard ratio, 1.36; 95% confidence interval, 0.97–1.90; $P = .08$). Finally, acute cellular rejection was not associated significantly with comorbidity. Thus, the CCI may be a practical tool for evaluation of comorbidity in these patients, but the relatively small sample size of this study and the fact that some of the comorbid conditions in the CCI lack the precision of using more transplant-related risk factors may dispute these results. Future studies are needed to clarify this concern.

Under this scenario, comorbidity is an important factor to determine patient survival after KT. Thus, the application of CI may be useful in predicting patient and graft survival in clinical trials and observational studies. Consequently, this may provide an objective, well-founded basis for decision making on the most appropriate therapeutic measures for kidney transplant recipients, thus helping to minimize mortality.

Acknowledgments

We thank the renal transplant team from the Canary Islands for their collaboration.

References

[1] Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003;108:2154-69.

[2] Ojo AO, Wolfe RA, Held PJ, et al. Delayed graft function: risk factors and implications for renal allograft survival. Transplantation 1997:968-74.

[3] Shoskes DA, Cecka JM. Deleterious effects of delayed graft function in cadaveric renal transplant recipients independent of acute rejection. Transplantation 1998;66:1697-701.

[4] Shoskes DA, Parfrey NA, Halloran PF. Increased major histocompatibility complex antigen expression in unilateral ischemic acute tubular necrosis in the mouse. Transplantation 1990;49:201-7.

[5] Irish WD, Mccollum DA, Tesi RJ, et al. Nomogram for predicting the likelihood of delayed graft function in adult cadaveric renal transplant recipients. J Am Soc Nephrol 2003;14:2967-74.

[6] Grossberg JA, Reinert SE, Monaco AP, et al. Utility of a mathematical nomogram to predict delayed graft function: a single-center experience. Transplantation 2006;81:155-9.

[7] Sanfilippo F, Vaughn WK, Spees EK, et al. The detrimental effects of delayed graft function in cadaver donor renal transplantation. Transplantation 1984;38:643-8.

[8] Cacciarelli T, Sumrani N, Delaney V, et al. The influence of delayed renal allograft function on long-term outcome in the cyclosporine era. Clin Nephrol 1993;39:335-9.

[9] Brier ME, Ray PC, Klein JB. Prediction of delayed renal allograft function using an artificial neural network. Nephrol Dial Transplant 2003;18:2655-9.

[10] Parikh CR, Jani A, Mishra J, et al. Urine NGAL and IL-18 are predictive biomarkers for delayed graft function following kidney transplantation. Am J Transplant 2006;6:1639-45.

[11] Shahbazian H, Mombini H, Moghaddam ZA, et al. Changes in plasma concentrations of hypoxanthine and xanthine in renal vein as an index of delayed kidney allograft function. Urol J 2006;3:225-9.

[12] Klabunde CN, Warren JL, Legler JM. Assessing comorbidity using claims data: an overview. Med Care 2002;40(8 Suppl):IV-26-35.

[13] Schneeweiss S, Maclure M. Use of comorbidity scores for control of confounding in studies using administrative databases. Int J Epidemiol 2000;29:891-8.

[14] Wright LF. Survival in patients with end-stage renal disease. Am J Kidney Dis 1991;17:25-8.

[15] Khan IH, Catto GR, Edward N, et al. Influence of coexisting disease on survival on renal-replacement therapy. Lancet 1993;341:415-8.

[16] van Manen JG, Korevaar JC, Dekker FW, et al. How to adjust for comorbidity in survival studies in ESRD patients: a comparison of different indices. Am J Kidney Dis 2002;40:82-9.

[17] Miskulin DC, Meyer KB, Martin AA, et al. Comorbidity and its change predict survival in incident dialysis patients. Am J Kidney Dis 2003; 41:149-61.

[18] Krakauer H, Bailey RC, Lin MJ. Beyond survival: the burden of disease in decision making in organ transplantation. Am J Transplant 2004;4:1555-61.

[19] Schneeweiss S, Seeger JD, Maclure M, et al. Performance of comorbidity scores to control for confounding in epidemiologic studies using claims data. Am J Epidemiol 2001;154:854-64.

[20] Hernandez D, Rufino M, Bartolomei S, et al. A novel prognostic index for mortality in renal transplant recipients after hospitalisation. Transplantation 2005;79:337-43.

[21] Jassal SV, Schaubel DE, Fenton SS. Baseline comorbidity in kidney transplant recipients: a comparison of comorbidity indices. Am J Kidney Dis 2005;46:136-42.

[22] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.

[23] Beddhu S, Bruns FJ, Saul M, et al. A simple comorbidity scale predicts clinical outcomes and costs in dialysis patients. Am J Med 2000;108: 609-13.

[24] Hemmelgarn BR, Manns BJ, Quan H, et al. Adapting the Charlson comorbidity index for use in patients with ESRD. Am J Kidney Dis 2003;42:125-32.

[25] Davies SJ, Philips L, Naish PF, et al. Quantifiying comorbidity in peritoneal dialysis patients and its relationship to other predictor of survival. Nephrol Dial Transplant 2002;17:1085-92.

[26] Jassal SV, Schaubel DE, Fenton SS. Predicting mortality after kidney transplantation: a clinical tool. Transpl Int 2005;18:1248-57.

[27] Wu C, Evans I, Joseph R, et al. Comorbid conditions in kidney transplantation: association with graft and patient survival. J Am Soc Nephrol 2005;16:3437-44.