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# A Logistic Regression Model for Predicting Health-Related Quality of Life in Kidney Transplant Recipients

H. Khedmat, G.-R. Karami, V. Pourfarziani, S. Assari, M. Rezailashkajani, and M.M. Naghizadeh

ABSTRACT

Background. To develop a logistic regression model capable of predicting health-related quality of life (HRQOL) among kidney transplant recipients and determine its accuracy.

Methods. Three groups of patients were selected: 70 healthy controls, 136 kidney transplant patients as a derivation set, and another 110 kidney transplant patients as a validation set. SF-36 score was used for HRQOL measurement. A cutoff point to define poor versus good HRQOL was calculated using the SF-36 scores of healthy controls. A logistic regression model was used to derive predictive parameters from the derivation set. The derived model was then tested among the validation set. HRQOL predictions made by the model for the patients in the validation set and the SF-36 scores were compared. We calculated sensitivity, specificity, positive and negative predictive values, and model accuracy.

Results. SF-36 scores below 58.8 were defined as an indication of poor HRQOL. The regression model suggested that poor HRQOL was positively associated with lower education (below high school diploma), being single or widowed, and diabetes/hypertensin as etiology. It was negatively associated with younger age (<45 years) at the time of transplantation. Optimal sensitivity and specificity were achieved at a cutoff value of 0.74 for the estimated probability of poor HRQOL. Sensitivity, specificity, positive and negative predictive values, and accuracy of the model were 73%, 70%, 80%, 60%, and 72%, respectively.

Conclusion. The suggested model can be used to predict poor posttransplant HRQOL among renal graft recipients using simple variables with acceptable accuracy. This modal can be of use in decision making in the recipients for whom achieving good HRQOL is the main aim of transplantation, to select high-risk patients and to start interventional programs to prevent a poor HRQOL.

HEALTH-RELATED quality of life (HRQOL) may be defined as a concept of personal satisfaction with health. It is described as a composite of several elements, including physical, psychological/spiritual, and socioeconomic well being.[1] HRQOL is increasingly recognized as an important outcome in renal transplantation.[2] However, the routine clinical use of standard HRQOL measurement tools is hindered by such barriers as the clinician's concern about feasibility,[2] cost, and time consumptions.[2] As an alternative, although some authors have tried to develop simple, quick-to-complete, and easy-to-score tools,[3] others suggest HRQOL prediction models.[4–9] Though like any other prediction tool, the value of predictions made by these models[3] entails evaluation of their validity and reliability.[10,11] These metrics have rarely been reported for the already devised HRQOL prediction models in renal transplantation.

Having shown improvements in HRQOL after renal transplantation, some case-control[12–14] and prospective

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studies[15,16] have suggested that there may be a chance of achieving HRQOL at the level of general population, even among all subscales of HRQOL.[17–19] Nevertheless, such improvements have not been achieved in certain cases.[6] Such failures to improve HRQOL after renal transplant contradicts the main reason to undergo a transplant, namely, the hope for improved posttransplant HRQOL.[20] Consequently, the prediction models that permit estimation of the probability of achieving a desirable HRQOL after renal transplantation can be used to inform high-risk patients. Therefore, it may be of help in pretransplantation decision making. In this study, we sought to develop and determine the accuracy of a logistic regression model capable of predicting HRQOL among kidney transplant recipients.

## METHODS

### Overview

A multiple logistic regression model was used to determine predictor variables associated with posttransplant HRQOL as the outcome and quantify these associations. A logistic regression model involves some independent (predictor) variables (nominal or continuous) that may be used to predict a dependent (outcome) binominal variable. As stated, the outcome we tried to predict using this regression model was poor HRQOL after renal transplantation. In fact, the model tried to compute the probability of obtaining a poor HRQOL after renal transplantation. The selected predictors were patient gender, age, marital status, age at transplantation, education level, monthly income, dialysis before transplantation, and duration/cause of end-stage renal disease (ESRD). These variables were assumed to have a role in predicting posttransplant HRQOL (outcome) in a renal transplant patient. We not only developed a prediction model but also tested the ability of this model to predict a poor HRQOL among a real group of kidney transplant patients. In brief, the following steps were taken: (1) selecting three groups of patients as healthy controls, derivation set (from whom the model parameters were derived), and a validation set (in whom the suggested model could be tested); (2) selecting a HRQOL measurement tool and defining a cutoff score for HRQOL among the healthy controls; (3) deriving model parameters from the derivation set; and (4) testing the derived model to see how well it predicted outcomes (poor HRQOL) using predictor variables among the validation dataset. Data analysis was performed using SPSS v. 13 for Windows. The study was approved by the ethics board and informed consent was obtained from all participants.

### Patients

Healthy controls included 70 people randomly selected from residents of Tehran. The derivation set consisted of 136 kidney transplant patients selected from several main transplantation centers in Tehran. The validation set included 110 kidney transplant patients from our center. Inclusion criteria for selection of both derivation and validation sets were clinically stable first-time kidney transplantations, with a functional kidney (serum creatinine $\leq$1.2 mg/dL in women and $\leq$1.4 mg/dL in men),[21] and at least 6 months after transplantation.[22] All groups were matched for age, gender, marital status, and educational level.

### HRQOL Measurement Tool and Defining a Cutoff Point

HRQOL of patients was measured using the 36-item Medical Outcome Study Short Form Health Survey (SF-36).[23] The SF-36 is a generic multidimensional measure of HRQOL that contains eight subscales representing physical functioning, social functioning, role limitations due to physical health problems, role limitations due to emotional problems, mental health, vitality, bodily pain, and general health perceptions. Subscale scores are transformed to 0 to 100 scales with higher scores indicating better HRQOL. The physical and mental components of the eight scales were combined into a physical composite score (PCS) and a mental composite score (MCS).[24] The SF-36 has proved reliable and valid in transplant patients.[25,26] The Farsi version of the SF-36 was used to ensure face validity and maximize acceptability in Iranian participants.[27,28] In this study, we used only total SF-36 score as the dependent variable; subscales and composite scores were not included. The SF-36 questionnaires were completed by the patients, but in some cases an interviewer's assistance was needed.

To define what SF-36 scores signified a poor HRQOL, we needed a cutoff point for SF-36 scores below which HRQOL could be considered poor. The 70 healthy controls filled the SF-36. Poor HRQOL was defined as having an SF-36 score below the first quartile of SF-36 scores among healthy individuals.

### Deriving Model Parameters From Derivation Set

The patients in the derivation set completed the SF-36 questionnaire. Using the cutoff value calculated in the previous step, the SF-36 scores of the patients in the derivation set were converted to a binominal outcome variable (poor/good HRQOL). A stepwise multiple logistic regression model was used to quantify associations between the assumed predictor variables and this binominal outcome variable. The input variables to the model (assumed predictors of HRQOL) included patient gender, age ($<$45 vs. $>$45 years), marital status (married vs. widowed/single), age at the time of the transplantation ($<$45 vs. $>$45 years), level of education (below vs. above high-school diploma), monthly family income (below vs. above 300 US$), positive history of dialysis before transplantation, duration of ESRD (in months), and the etiology of ESRD, namely diabetes mellitus (DM) or hypertension (HTN) versus other etiologies. It is noteworthy that all predictor variables were input to the model as categorical variables except for ESRD duration. The significance level for each variable's entry to or removal from the model was set at .1.

### Testing the Derived Prediction Model in Validation Set

The kidney transplant patients in the validation set were asked to complete the SF-36 questionnaire. Using the cutoff value calculated, their HRQOL were categorized as poor or good. Then the model derived in the previous step was used to predict poor HRQOL among these patients. We compared the HRQOL predictions made by the model for patients in validation set and the SF-36 scores. We calculated the sensitivity, specificity, positive/negative predictive values, and model accuracy.

The definitions used to calculate the indices related to model validation were true positives (TP)—the number of patients the model correctly predicted as poor HRQOL; false positives (FP)—the number of the patients with good HRQOL the model falsely predicted as poor HRQOL; true negatives (TN)—the number of the patients the model correctly predicted as good HRQOL; and

false negative (FN)—the number of the patients with poor HRQOL the model wrongly predicted as good HRQOL. Then the following formulae were used to calculate the indices related to model validation: sensitivity = TP/(TP + FN); specificity = TN/(TN + FP); positive predictive value (PPV) = TP/(TP + FP); negative predictive value (NPV) = TN/(TN + FN), and accuracy = (TP + TN)/(TP + FP + TN + FN).

The model suggested by regression analysis estimated different probability values to predict poor HRQOL that may vary with the predictor values for each patient. However, it will be useful to know how valid each of these predicted probability levels can be as cutoff points to screen patients with poor HRQOL. For instance, if we arbitrarily set the cutoff probability to .80 as the one above which we define a patient as one ending up with a poor HRQOL, then we wish to know the answers to the following two questions: (1) How sensitive is the model at this cutoff value? In other words, what proportion of the patients who really have a poor HRQOL in the validation dataset will be present among the patients the model predicted as having poor HRQOL, that is, those with an estimated probability >.80 in this arbitrary example? (2) How specific is the model at this cutoff, or in other words, what proportion of patients who truly have a good HRQOL in the validation dataset will be present in the group the model predicted to have good HRQOL? To clarify this, sensitivity and specificity curves were plotted for different levels of the probabilities the model estimated. This was then used to find the model-estimated probability cutoff, at which we achieved optimal sensitivity and specificity namely, maximal sum of sensitivity and specificity point of crossing.

**Table 1. Comparison of Input Variables in Patients With Poor and Good HRQOL Among Patients in the Derivation Set ($n$ = 136)**

| Predictor Variable | Poor HRQOL, *n* (%) | Good HRQOL, *n* (%) | *P*-Value |
|---|---|---|---|
| Gender | | | |
| Male | 64 (67.4) | 31 (32.6) | .472 |
| Female | 25 (61) | 16 (39.0) | |
| Education | | | |
| Below high school diploma | 53 (76.8) | 16 (23.3) | .005 |
| Above high school diploma | 36 (53.7) | 31 (46.3) | |
| ESRD etiology | | | |
| HTN/DM | 41 (55.4) | 33 (44.6) | .009 |
| Others | 47 (77.0) | 14 (23.0) | |
| Monthly family income | | | |
| <US$ 300 | 84 (68.3) | 39 (31.7) | .031 |
| >US$ 300 | 5 (38.5) | 8 (61.5) | |
| Age at transplantation | | | |
| <45 years | 59 (60.2) | 39 (39.8) | .039 |
| >45 years | 30 (78.9) | 8 (21.1) | |
| Marital status | | | |
| Single/widowed | 23 (69.7) | 10 (30.3) | .555 |
| Married | 66 (64.1) | 37 (35.9) | |
| Dialysis before transplantation | | | |
| No | 15 (71.4) | 6 (28.6) | .530 |
| Yes | 74 (64.3) | 41 (35.7) | |
| | Mean ± SD | Mean ± SD | |
| ESRD duration | 64.5 ± 80.6 | 64.7 ± 77.2 | .998 |
| Age | 41.2 ± 10.9 | 37.6 ± 13.3 | .115 |

The SF-36 total score cut-off point for defining poor HRQOL was 58.85.
*Abbreviations:* DM, diabetes mellitus; ESRD, end-stage renal disease; HRQOL, health-related quality of life; HTN, hypertension.

**Table 2. The Input Variables in the Model That Were Recognized as Significant Predictors of Poor HRQOL in Multiple Logistic Regression Analysis for the Patients in Derivation Set**

| | $\beta$ | *P* Value | OR | 90% CI |
|---|---|---|---|---|
| ESRD etiology (not DM/HTN) | 1.108 | .003 | 3.027 | 1.631–5.616 |
| Education (above high school diploma) | 1.017 | .004 | 2.764 | 1.537–4.972 |
| Marital status (married) | 1.009 | .034 | 2.743 | 1.254–6.000 |
| Age at transplantation (>45 yrs) | −0.685 | .036 | 0.504 | 0.295–0.863 |

*Abbreviations:* CI, confidence interval; DM, diabetes mellitus; ESRD, end-stage renal disease; HRQOL, health-related quality of life; HTN, hypertension; OR, odds ratio.

## RESULTS

The mean value ± SD of age was 37.9 ± 10.9, 39.6 ± 13.8, and 40.8 ± 14.1 years in controls, derivation set, and validation set, respectively. The number of male and female subjects were 48 (68.5%) and 22 (31.5%) in the control group; 171 (67.6%) and 32 (32.4%) in the derivation set; and 76 (68.5%) and 35 (31.5%) in the validation set. The mean time interval between transplantation and HRQOL assessment was 3.0 ± 2.2 years in the derivation set and 3.5 ± 2.5 years in the validation set.

The first, second, and third quartiles of the SF-36 total scores in 70 healthy controls were 58.8, 63.3, and 67.5, respectively. The SF-36 scores below 58.8 were defined as an indication of poor HRQOL. The multiple logistic regression analysis suggested a statistical equation to predict poor HRQOL:

$$\text{logit}(P) = 1.108*\text{ESRD} + 1.017*\text{EL} + 1.009*\text{MS} - 0.685*\text{A} \quad (1)$$

In this equation, $P$ stands for the probability of poor HRQOL; ESRD means DM or HTN as a cause for ESRD; EL, education level; MS, marital status; and A, age at the time of transplantation. ESRD is valued 1, if the cause of ESRD is either DM or HTN, and 0 for other causes. EL is valued at 1, if the education level is under high school diploma and 0 if above. MS is valued at 1 if the patient is single or widowed, and 0 if married. Age is valued at 1 if the patient was younger than 45 at the time of transplantation and 0 if older. In fact, logit($P$) is equal to $\ln(P/1-P)$, and thus $P$ can be calculated from logit($P$).

Table 1 compares the input variables among patients with poor versus good HRQOL in the derivation set. The input variables recognized by regression analysis as statistically significant predictors of HRQOL (among the patients in derivation set) are listed in Table 2. In brief, the model showed that the estimated probability of HRQOL after transplantation was a function of age at the time of

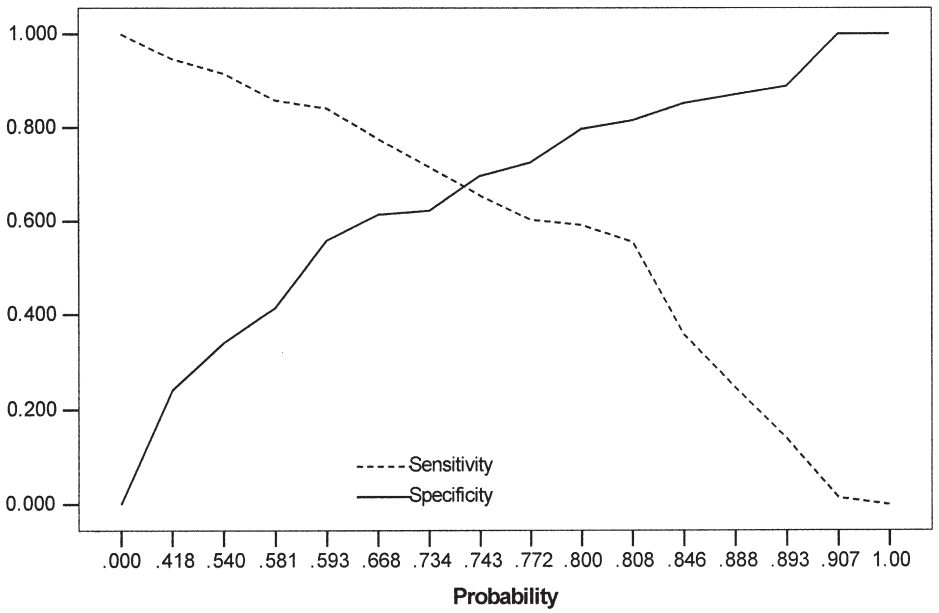


**Fig 1.** Sensitivity and specificity trends for the different cutoff values of the estimated probability of poor HRQOL predicted by the model for the validation set. Sensitivity and specificity were calculated using the SF-36 scores of the validation set (scores < 58.85 were considered poor HRQOL). Optimal sensitivity and specificity was achieved at a cut-off value of 0.74. See text for details.

transplantation, marital status, educational level, and DM/HTN as the etiology of ESRD. Poor HRQOL was positively associated with lower education (below high school diploma), being single or widowed, and DM/HTN as the etiology of patient's ESRD; and negatively associated with younger age (<45 years) at the time of transplantation.

Point crossing plot of sensitivity and specificity curves (Fig 1) showed that the maximum sum of the sensitivity and specificity was achieved at a cutoff model-estimated probability of poor HRQOL of .74. Therefore sensitivity, specificity, PPV, NPV, and accuracy of the model were 72.9%, 70%, 80.1%, 59.6%, and 71.8%, respectively.

Table 3 shows the results from validation set after setting the cutoff point at .74 (the point where optimum sensitivity and specificity were reached). Of total 70 patients with poor HRQOL (determined by the SF-36 scores), the model correctly predicted 51 (true positives; sensitivity, 72.9%), but failed in 19 (27%) subjects. Of the total 40 patients with good HRQOL, the model correctly predicted 28 (true negatives; specificity, 70%), and wrongly predicted 12 (30%). In fact, one can get a table like Table 3 for every level of the estimated probability of poor HRQOL resulting in different levels of model accuracy indices.

**Table 3. Comparison of the Number of the Patients With Poor/Good HRQOL Predicted by the Model and Measured by SF-36 in Validation Set**

| | HRQOL Predicted by the Model | | |
|---|---|---|---|
| | Good | Poor | Total |
| HRQOL measured by SF-36 | | | |
| Good | 28 | 12 | 40 |
| Poor | 19 | 51 | 70 |
| Total | 47 | 63 | 110 |

This table was used to calculate sensitivity, specificity, and other indices related to accuracy of the model. The probability cutoff used for categorizing the patients predicted by the model was 0.74; the cutoff value found for optimal sensitivity and specificity (see Fig 1).

*Abbreviation:* HRQOL, health-related quality of life.

## DISCUSSION

Herein we have presented a prediction model with acceptable accuracy for poor post-renal transplant HRQOL using simple input variables. Prediction of HRQOL in renal transplant subjects offers multiple advantages. First, this prediction may positively influence patients' feelings, especially considering the increased life expectancy associated with renal transplantation.[29] Second, pretransplant prediction of HRQOL can be a great help for patient decision making, considering the fact that achieving a good HRQOL is the primary reason for which many patients opt for a renal transplantation. Third, there is evidence showing a correlation between poor HRQOL and treatment noncompliance,[7,30] which in itself is associated with allograft rejection and death.[31] A prediction tool can screen, before transplantation, the subjects at high risk of having a poor posttransplant HRQOL. This tool will enable physicians to consider appropriate interventional programs for HRQOL improvement well in advance, and therefore may indirectly aid in preventing graft rejection in some patients.[32] Fourth, such prediction models are easier to use and less time consuming compared with standard HRQOL instruments, thus facilitating estimation of HRQOL for some physicians who do not usually use standard HRQOL instruments in their routine practice.[33]

Our logistic regression model showed that the estimated probability of HRQOL after transplantation was a function

of age at the time of transplantation, marital status, educational level, and DM/HTN as the etiology of ESRD. One review categorized HRQOL predictors among renal transplant patients into three groups including reduction in adverse events, facilitation of employment, and enhancement of social support.[4] Numerous variables have been suggested by other studies as predictors of HRQOL in renal transplant patients. The number of hospitalization days, employment status, and social support has been recognized as the main predictors of HRQOL.[6] This long list of variables used in different models also contains such variables as social support, sociodemographic and clinical variables, side effects of medications, and compliance to them,[34] recipient age, donor age, medications, source of graft, number of HLA mismatches, length of cold ischemia time, known comorbidity, pretransplant dialysis, previous renal transplantation, serum creatinine at inclusion, previous antihypertensive treatment,[5] age at transplantation, term of hemodialysis, gender, hypertension, acute rejection, and serum levels of creatinine.[8] However, among all these reported variables, we used several simple predictors as the input variables of our prediction model. Although omission of a number of the numerous variables may seem a flaw in the model, it has the advantage of making our prediction model simple and easy to use.

Finally, a major advantage of our model lies in its acceptable accuracy, which was validated in this study. Previously reported prediction models have not reported the validity of their models.[5,6,8,34] The acceptable accuracy of our model in our setting may increase the acceptance of the model by nephrologists and encourage them to rely on the prediction equation suggested by our model. If this model can be validated in diverse settings, it can be a handy tool to those clinicians who have difficulty using the conventional time-consuming HRQOL standard measures.

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