Predicting graft survival among kidney transplant recipients: A Bayesian decision support model

Kazim Topuz [a], Ferhat D. Zengul [b], Ali Dag [c], Ammar Almehmi [d], Mehmet Bayram Yildirim [e],*

[a] Division of Management Information Systems, Price College of Business, University of Oklahoma, USA
[b] Department of Health Services Administration, University of Alabama at Birmingham, USA
[c] Beacom School of Business, University of South Dakota, USA
[d] Interventional Nephrology Program, University of Alabama at Birmingham, USA
[e] Department of Industrial, Systems and Manufacturing Engineering, Wichita State University, USA

ABSTRACT

Predicting the graft survival for kidney transplantation is a high stakes undertaking considering the shortage of available organs and the utilization of healthcare resources. The strength of any predictive model depends on the selection of proper predictors. However, despite improvements in acute rejection management and short-term graft survival, the accurate prediction of kidney transplant outcomes remains suboptimal. Among other approaches, machine-learning techniques have the potential to offer solutions to this prediction problem in kidney transplantation. This study offers a novel methodological solution to this prediction problem by: (a) analyzing the retrospective database including >31,000 U.S. patients; (b) introducing a comprehensive feature selection framework that accounts for medical literature, data analytics methods and elastic net (EN) regression (c) using sensitivity analyses and information fusion to evaluate and combine features from several machine learning approaches (i.e., support vector machines (SVM), artificial neural networks (ANN), and Bootstrap Forest (BF)); (d) constructing several different scenarios by merging different sets of features that are optioned through these fused data mining models and statistical models in addition to expert knowledge; and (e) using best performing sets in Bayesian belief network (BBN) algorithm to identify non-linear relationships and the interactions between explanatory factors and risk levels for kidney graft survival. The results showed that the predictor set obtained through fused data mining model and literature review outperformed the all other alternative predictors sets with the scores of 0.602, 0.684, 0.495 for F-Measure, Average Accuracy, and G-Mean, respectively. Overall, our findings provide novel insights about risk prediction that could potentially help in improving the outcome of kidney transplants. This methodology can also be applied to other similar transplant data sets.

© 2017 Elsevier B.V. All rights reserved.

1. Introduction

Organ transplantation has the potential to provide a better quality of life for patients and improve their survival [1]. According to the World Health Organization (WHO), of the 119,873 organ transplants worldwide, 67% are kidney transplants, and 59% of those are from deceased donors [2]. Due to the shortage in the supply of kidneys, the waiting time to receive a kidney transplantation in dialysis patients is long and arduous. Also, a substantial number of kidney transplantations fail due to graft rejection, which is attributed primarily to chronic allograft rejection related to an inefficient match between donor and recipient [3]. Failures in the transplant process create a dual effect: first, they result in the loss of a viable organ in a time where organ shortage and lengthy wait-times are already a severe issue. Second, the economic effect of a failed transplant, combined with the patient's return to dialysis or the transplant wait-list results, is a burden on the transplant system, healthcare system, and the patient's quality of life. Therefore, in addressing these failures, improvements in the predictive models of graft survival have a positive compounding effect. Even a slight improvement in predictions has the potential to improve the long-term survival of a kidney graft, thus benefiting the recipient's quality of life and increasing the efficient use of healthcare resources in an industry mired with inefficiency.

Predicting graft survival is vital for efficiency in transplant success since it both enables an increase in the utility of the available pool of organs and benefits the healthcare system's resource utilization. Graft survival refers to the length of time that a transplanted kidney (graft) functions to the degree that the patient does not need dialysis or another transplant [3]. Although considerable research has analyzed the clinical predictors of survival in transplant patients [4–9], few studies have attempted to use machine-learning approaches in the kidney transplant

population to predict outcomes [6,8,9]. Recent studies have shown that machine-learning models perform reasonably well in predicting graft survival and identifying contributing factors that are not part of current domain knowledge [6]. However, few studies have thoroughly examined the conditional relations among significant predictors or have identified the patient-specific risk category of kidney transplantation [9,10].

In machine-learning methods, probabilistic graphical models (PGMs) play a major role in modeling the complex nonlinear relations among different variables and reasoning under uncertainty [11]. Bayesian belief networks (BBNs) have become popular among PGMs because they can handle previously unknown but potentially useful information embedded in networks. Few studies have developed BBN models in organ transplantation using various survival time frames: kidney (1–3 years) [9] and liver (90 days) [5]. However, current BBN studies of the renal transplantation population have used either relatively smaller and older data sets (i.e., Li et al. [10]), or evaluated kidney transplantation outcomes using a single-center database (i.e., Brown et al. [9]). The ever-increasing amount of data and the continuous addition of new potential predictors into existing data sets demand the use of better, more comprehensive methodologies in extracting useful knowledge from the data. Increased data and predictors require better feature-selection techniques and methodologies that can incorporate existing domain knowledge into new data sets. Leveraging the massive amounts of data collected on patients can lead to better prediction models, which will enable data-driven decision support tools for decision makers and domain experts, augment their knowledge to create better outcomes for patients, and increase efficiency for resource usage in the healthcare industry.

To this effect, the primary goal of this study is to create a comprehensive methodology that combines exhaustive variable selection with machine learning techniques to enable better predictive abilities and identification of important factors that contribute to the risk of graft failure and the probabilistic dependencies among them. To achieve this goal, we apply a novel, comprehensive methodology on kidney graft survival data to predict graft survival and identify contributing factors and patient-specific risk. We have used statistical approaches, such as elastic nets (ENs) combined with machine-learning approaches such as artificial neural networks (ANNs), bootstrap forest (BF), and support vector machines (SVMs) to select essential predictors in the data. These predictors are used to construct a Bayesian belief network for multinomial prediction. The findings from the BBN model are then used to extract hidden conditional dependencies among the different variables.

This study contributes to the graft survival prediction literature by doing the following: (a) developing a comprehensive variable selection framework and creating a multiclass prediction model for accurate prediction, (b) providing insights into important factors leading to graft failure, (c) identifying interactions between explanatory/preoperative factors and risk levels, and (d) performing a patient-specific risk analysis.

We have organized our work in this paper as follows: In Section 2, we provide an overview of existing literature on the topic of graft survival risk prediction with a cursory focus on kidney transplantation in order to provide the reader with a basis with which to compare our proposed methodology; in Section 3, we discuss the methods and analytic framework used in this study; in Section 4, we provide the results of our study; and finally, in Section 5, we discuss the results, limitations, and implications for decision makers, as well as provide some suggestions for future research.

2. Background

The ability to predict the post-transplant graft survival after a transplant is one of the key factors in the donor-recipient matching procedure. This matching is critical because the supply of donor organs is limited. An extensive body of research has used data-driven methods to predict post-transplantation graft survival [6,9,12]. These methods can be classified as follows: (a) simulation and operations research, (b) conventional statistics, and (c) data analytic approaches.

Simulation-based organ transplantation studies have a long history [13]. Ruth et al. [14] designed a discrete simulation model to evaluate the impact of the availability of deceased kidney donors on post-transplantation graft survival using state-level data in Michigan [14]. Both blood type and tissue compatibility were included in the matching process. Later studies proposed simulation models for different organs: liver [15], heart-lung [16], and kidney-pancreas [17]. In order to improve the organ transplant matching algorithms, several operations management and research studies have utilized various optimization models and Markov decision models [18–21]. However, the major drawback of these investigations was limiting the matching process to a small number of variables, such as the functional status of the recipient and some donor-recipient characteristics (e.g., blood type).

Conventional statistical studies, including Kaplan-Meier estimates and Cox proportional hazards models, have been used extensively in the medical literature of organ transplantation [4,22–24]. In fact, beginning in 1987, Rana et al. [24] used the Kaplan-Meier survival function to provide an overview of organ (including kidney) transplantation survival. Several other studies have analyzed the effect of patient characteristics (age, sex, and race) [23] and preoperative transplant factors (human leukocyte antigen matching, donor type, cold ischemia time acute rejection, functional status of a graft after transplant) [22,25] on graft outcomes by using the Kaplan-Meier survival function. However, similar to previous analyses, these studies were limited by utilizing a small number of candidate predictors. Accordingly, there is a need to use larger data sets that include a greater number of variables to unmask potential hidden patterns among the different variables, which could affect the clinical outcomes of a kidney transplant. As such, the present study sought to utilize data analytic approaches using scores of candidate predictors to examine the conditional dependency among a large set of variables. While this research uses a kidney transplant graft survival data set, studies of other organ transplants are also highlighted in this literature review, because the methodology proposed in this study is applicable to any transplant data set, and as such, a comparison to current works in this domain is provided for the reader's benefit.

Data mining-based techniques (DTs) can be classified into two groups: one focusing only on accurately predicting the post-transplantation graft survival by identifying the most significant predictors [4,25,26], and the other concentrating on extracting the conditional relations among the significant predictors and then identifying the patient-specific category of survival. As an example of the first group of studies, Kusiak et al. [26] compared the effectiveness of two DTs—decision trees and rough sets (RSs)—in predicting the survival of 188 kidney dialysis patients. Although the results of both methods were accurate, it is not clear whether this approach applies to a larger data set. In another study, DTs were also used to predict the prognosis of acute liver failure to enhance the inclusion criteria for liver transplants [27]. To broaden the prediction variables, Akl et al. [8] used demographic, clinical, and pharmaceutical data to compare the performance of an ANN and a statistically derived nomogram in predicting the five-year graft survival after a kidney transplant. They found that the ANN model outperformed the statistically derived nomogram on an external validation data set. In another study, Lin et al. [25] determined the effect of various predictors on the one- to seven-year kidney survival rate using logistic regression, the Cox proportional hazard model, and multiple-output ANNs. Dag, Oztekin, Yucel, Bulur and Megahed [28] used four classification algorithms (decision trees, ANNs, SVMs and logistic regression) to classify graft survival for heart patients at one, five, and nine years. They used data-balancing algorithms (SMOTE and RUS) to tackle the imbalanced nature of the data. Their study showed that logistic regression coupled with SMOTE gave the best outcome prediction on test data, with area under the curve (AUC) values of 0.624, 0.676, and 0.838 for one-, five-, and nine-year survival, respectively. Oztekin, Kong and Delen [29] used a structural