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# Application of Artificial Neural Networks in Renal Transplantation: Classification of Nephrotoxicity and Acute Cellular Rejection Episodes

A.D. Hummel, R.F. Maciel, R.G.S. Rodrigues, and I.T. Pisa

ABSTRACT

Complications associated with kidney transplantation and immunosuppression can be prevented or treated effectively if diagnosed in the early stages by posttransplant monitoring. One of the major problems is diseases that occur during the first year after kidney transplantation. For this purpose, we used different classifiers to predict events of nephrotoxicity versus acute cellular rejection episodes. The classifiers were evaluated according to values of sensitivity, specificity and area under ROC curves (RCA). The classifier with better accuracy rate for nephrotoxicity achieved the value of 75.68% and RCA classifier reached the accuracy of 80.89%. These results are encouraging, with rates of accuracy and error consistent with work purpose.

BETWEEN THE 1980 and 1990 the number of transplants has increased in several countries.[1] Paradoxically the transplant waiting list has also grown because the number of potential recipients in greater than the number of donors. There is also the difficulty of finding a compatible donor for the recipient.[2] Because of these issues there is an emerging problem of waiting list mortality.[3] Furthermore, the chronic use of immunosuppressants is a problem due to their nephrotoxicity that can result in loss of kidney function.[4]

Improvements in organ transplantation seek to reduce failure rates and improve patient life quality, using statistical analysis,[5] mathematical models,[2,6] and artificial intelligence techniques.[7] The aim of these methodologies is to improve process understanding[2] or to detect appropriate profiles of recipients that will have a greater survival chance. These techniques contribute directly or indirectly to the discovery of new knowledge.[7] The objective of this work was to obtain a pattern classifier using artificial neural networks (ANN) that determined nephrotoxic events of immunosuppressors (Nephrotoxicity) versus acute cellular rejection episodes (ARE).

## METHODS

The database in this study measured the occurrence of the nephrotoxicity versus ARE over the first posttransplant year. The data were collected on 145 patients who displayed the inclusion criteria of any suspicion of nephrotoxicity or ARE with a concomittant biopsy. We excluded patients who did not use a calcineurin inhibitor. This study was approved by our Research Ethics Committee (Process numbers 1677/08 and 2554/09.)

The variables were consultation time after transplantation, tacrolimus dose, induction therapy, renal initial function, donor type, cytomegalovirus (CMV) in the recipient, diuresis, temperature increase, edema, tremor, urea dosage, serum creatinine, blood glucose, leukocyte count, lymphocyte count, platelet count, AT average, and histocompatibility. Weka software was used to generate the ANNs, resulting in 1456 different ANN models for nephrotoxicity and ARE. Therefore, we varied its topology with the following parameters: number of neurons in the hidden layer, random seed, learning rate, decay rate. This work included a training and a test method with 4-fold cross validation. The accuracy between methods was compared by accuracy (ACC), sensitivity (SEN), specificity (ESP), and area under the ROC curve (AUC).

## RESULTS

The classifier with better accuracy rate for nephrotoxicity achieved the value of 75.68% (SEN, 24%; ESP, 96.39%; AUC, 0.64) and better sensitivity with the value of 49% (ACC, 71.91%; ESP, 81.06%; AUC, 0.66) (see Table 1). On the other hand; ARE classifier reached the best performance in accuracy in

From the Programa de Pós-graduação em Informática em Saúde (A.D.H.), Universidade Federal de São Paulo (UNIFESP); the Programa de Pós-graduação em Saúde Coletiva (R.F.M.), UNIFESP; the Laboratório de Instrumentação e Acústica (R.G.S.R.), Universidade de Ciências da Saúde de Alagoas, Maceió – AL; and the Departamento de Informática em Saúde (I.T.P.), UNIFESP, São Paulo, Brazil.

Address reprint requests to Rafael Fabio Maciel, Rua Botucatu, 862, Vila Clementino, São Paulo, SP, Brazil, CEP: 04023-900. E-mail: rfmaciel@uol.com.br



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**Table 1. Evaluation of Classifiers Nephrotoxicity and ARE**

| Database | ACC (%) | SEN | ESP | AUC |
|---|---|---|---|---|
| Nephrotoxicity ACC | 75.68 | 0.24 | 0.96 | 0.64 |
| Nephrotoxicity SEN | 71.91 | 0.49 | 0.81 | 0.66 |
| ARE ACC | 80.89 | 0.62 | 0.88 | 0.66 |
| ARE SEN | 80.00 | 0.63 | 0.87 | 0.78 |

80.89% (SEN, 62.67%; ESP, 88.83%; AUC, 79.21), and the best sensitivity in 63.17% (ACC, 80%; ESP, 87.32%; AUC, 0.78). More information about the classifiers used in this study can be found in http://telemedicina6.unifesp.br/projeto/artigo/transplantationproceedings.html.

## DISCUSSION

The classification results were considered significant by experts who evaluated the classifiers. However, higher rates of sensitivity will be required to apply the classifier in clinical practice, which would allow, for example, the development of an automatic screening tool for biopsy. Therefore, the next steps of this research are validation of pattern classifiers with other transplant patients from the same service, and conduct of experiments with other techniques of data mining seeking to increase the classifier sensitivity. Is noteworthy that no studies were found which apply data mining techniques, as ANNS, to the classification of nephrotoxicity and ARE.

In conclusion, although the results are encouraging, more studies are necessary to deploy automatic classifiers of nephrotoxicity and ARE in clinical practice.

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