Getting the most out of your data using artificial intelligence: from bench to bedside in transplantation

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Transplantation and nephrology have generated substantial data over the last decade, including omics, clinical, or electronic medical data. Genomic, transcriptomic, proteomic, and metabolomic data can be gathered from various biological samples, such as serum, blood, urine and tissue biopsies. Furthermore, data from registries are almost universal for all employed in the field of transplantation. Bringing together multi-omics data with the clinical electronic medical data sets and defining the statistical approach to harmonize them poses a considerable challenge.

Machine learning in nephrology

In the field of nephrology and transplantation, in particular, machine learning is an analytical technique that addresses the issue of data prediction. It can be broadly divided into supervised and unsupervised learning. To predict outcomes with known classes, supervised learning often employs a statistical technique that involves training the data set with known class labels. To the contrary, with unsupervised learning, both the class labels and data are unorganized, leaving it to the researcher and algorithm to identify the data structure and other patterns throughout the entire data set.

One example of unsupervised machine learning is clustering. The team led by Drs Jean Yang and Germaine Wong from the University of Sydney used an unsupervised machine learning model on a data set for over 100 different variables collected from a screening test diagnostic study from around 1700 CKD, dialysis and transplant patients. The entire data set can be visualized in a three-dimensional platform, with a representation of individual variables placed into individual categories, such as demographics, medications and comorbidities. The outcomes of interest and the different variables are joined together and can be clustered into specific characteristics, so that different factors may predict the outcomes of interest.

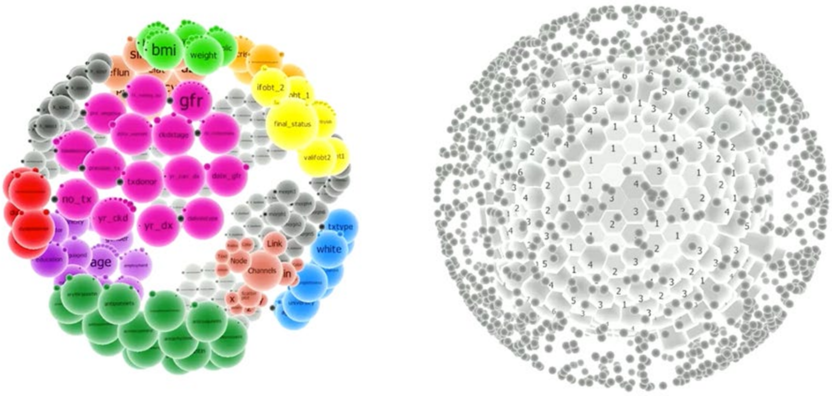

Figure 1. Unsupervised machine learning - data visualization

The data can also be handled using production modelling, a type of traditional supervised machine learning. In this case, the training data set and testing data set each contain different sets of data. The objective is to perceive the key features that characterize outcome predictors. The machine uses the training data set to create an algorithm that will be used to forecast a new set of data, and then it tests if the new set of data performs as well. The discrimination platform, which includes the learning set (data with known classifications) and the classification method, serves as the foundation for predictive analysis. Applying the classification rule initiates the prediction process, which then establishes the class assignment. However, the question remains of how to ascertain the most reliable concept. Thus, cross-validation is the approach of choice. The data are randomly divided into the testing and training sets and run into multiple faults. The error rate is calculated individually for each dataset. In this way, the data is considerably different after resampling, and the collection of error rates is generated over time. Afterwards, the average patient accuracy is computed, depending on the number of times the sample was tested, until stability is achieved.

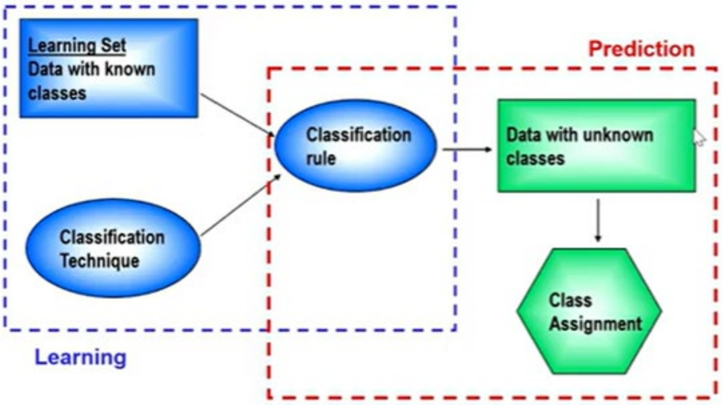

Figure 2. Process of classification, machine learning and predictive analysis

Dr Yunwel Zhang used supervised and unsupervised learning techniques with clinical data to address the issue of heterogeneity in transplant survival outcomes between patient groups. First, patients were divided into distinct homogenous groups with unique characteristics for each subgroup using ensemble clustering. Researchers were able to describe graft and patient survival in detail within each distinct category, allowing them to examine prediction in a more individualized way than in a population-based one. Fairness considerations must be accounted for at each step of a model's life cycle. Therefore, it is essential to obtain data from different sources, i.e., from different people with various ethnic, gender and age groups, to develop a model that applies to everyone and also a viable validation process.

Coorey et al. presented prediction modelling using machine learning strategies to improve transplantation outcomes and summarized all the potential techniques that can be used in clinical medicine clustering methods, including PCA factor analysis, k-means clustering, decision tree, random forest and SVG clustering. Yi et al. constructed a deep-learning-based pipeline to classify normal and abnormal kidney allograft tissue compartments and mononuclear leukocyte infiltrates. Periodic acid– Schiff-stained slides of transplant biopsies (60 training and 33 testings) were used to identify critical or important histological pathologies including scarring and chronic rejection. The algorithm was validated using data from the Westmead PTA Scale data and a relatively good performance was found in determining the chronic Banff score and predicting the 12-month death-censored graft survival.

Artificial intelligence in transplantation nephrology

One of the major challenges with transplantation is to define good prognostic markers that would help identify patients at risk of graft rejection, and to timely adjust the immunosuppression therapy. However, no biomarker is perfect. One set of biomarkers derived from a single data cohort may not necessarily perform well in another. The research group led by Yue Cao performed a meta-analysis of the geodatabase that looked at biomarkers in both short- and long-term transplantation outcomes. Key genes from each specific data set were selected and combined using a range of different machine-learning methods. The results showed that a set of gene signatures for acute rejection derived from a specific cohort of kidney transplant recipients did provide adequate prediction in an independent cohort of transplant recipients. Nevertheless, the integration of gene signature sets with high specificity scores may improve the prediction performance of these markers.

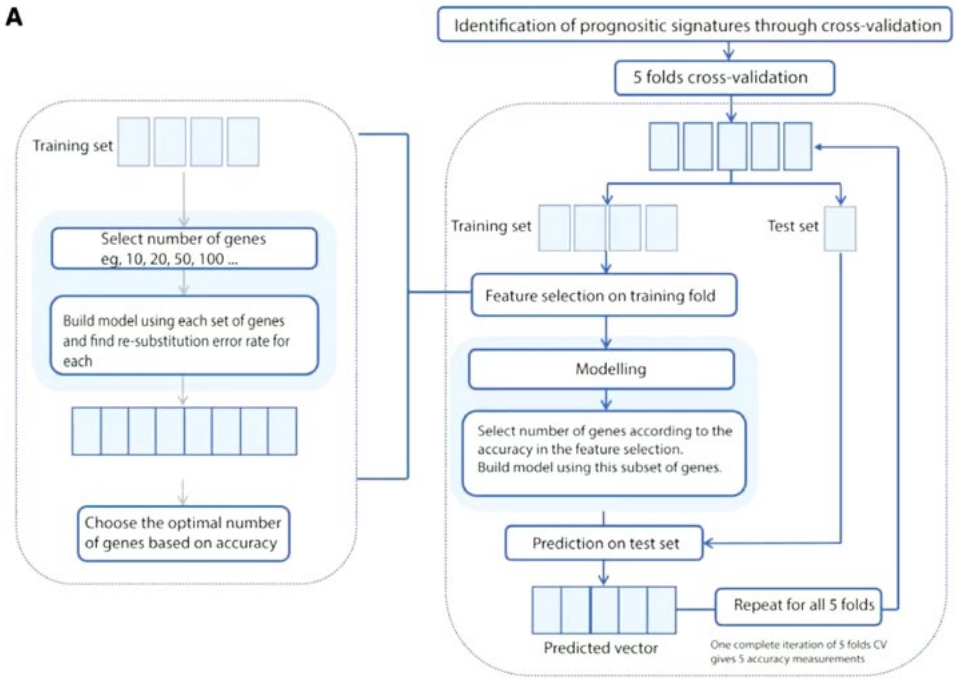

Figure 3. Prognostic biomarkers in kidney transplantation

A study by Yingxin Lin et al. used four different machine learning methods, both supervised and unsupervised, and observed the non-utilization of kidneys from donors after circulatory determinant of death (DCDD). Self-organizing maps were used to group these donors into clusters with similar characteristics and features associated with non-utilization were defined. This work not only aimed to define the prediction factors but also to address the issues of the consistency, transparency and accuracy of the machine learning methods used. Decision tree, Logistic regression and Random Forest methods all found similar predictive elements which included terminal creatinine, as well as the withdrawal time from cardiopulmonary arrest. Using the Self-organizing map, researchers were able to group the factors into nine separate clusters and found consistent results for both supervised and unsupervised learning algorithms.

Key points

1. Artificial intelligence is transforming the field of renal transplantation and machine learning is gaining a lot of attention in this area.
2. Methods to evaluate model performance must be robust. The issue of heterogeneity is important since it addresses the issues of fairness and equity.
3. Consistency and transparency in reporting the Machine Learning methods are of utmost importance.

Further reading

1. Bontha SV, Maluf DG, Mueller TF, Mas VR. Systems Biology in Kidney Transplantation: The Application of Multi-Omics to a Complex Model. *Am J Transplant*. 2017;17(1):11-21. doi:10.1111/ajt.13881
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3. Yi Z, Salem F, Menon MC, et al. Deep learning identified pathological abnormalities predictive of graft loss in kidney transplant biopsies. Kidney Int. 2022;101(2):288-298. doi: 10.1016/j.kint.2021.09.028.
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5. Lin Y, Teixeira-Pinto A, Opdam H, et al. Nonutilization of Kidneys From Donors After Circulatory Determinant of Death. Transplant Direct. 2022;8(6):e1331. doi: 10.1097/TXD.0000000000001331.