Title: Prediction of cardiac surgery associated AKI using machine learning and noninvasive urine oxygen monitoring

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Background: Acute kidney injury (AKI) is a common complication of cardiac surgery.[1] Due to lack of therapies that enhance renal recovery current clinical care focuses on injury prevention. However, current diagnostic tools, as defined by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, do not have prognostic value.[2,3] Researchers have shown certain biomarkers demonstrate good discriminatory ability with an area under the receiver operator characteristic curve (AUROC) ranging from 0.7 to 0.8.[4] These biomarkers have limited clinical utility as they require expensive equipment and do not provide immediate results. Recently, researchers have focused on the partial pressure of oxygen in the urine (PuO_2) as a physical biomarker of AKI because it has been shown that renal hypoxia plays an early role in the development of the disease.[5] While studies indicate PuO_2 may be useful for identifying patients who develop AKI there are no real-time algorithms which could be incorporated into a PuO_2 monitor.[6] Thus, the aim of this research was to develop an algorithm based on intraoperative PuO_2 and patient characteristics to predict post-operative AKI.

Methods: Second-by-second intraoperative PuO_2, body mass index (BMI) and baseline serum creatinine values were collected in 86 cardiac surgery patients.[6] Patients were diagnosed with AKI based on the urine output and serum creatinine KDIGO criteria. These data were used to train and test 3 machine learning algorithms: a support vector machine ensemble with bagging, CatBoost (gradient boosted decision trees), and a fully connected neural network.[7] The data were split into training and testing groups, stratified by stage of AKI diagnosis. To identify the best set of hyperparameters 10-fold cross-validation was performed using only the training data. The AUROC was averaged across all 10 folds for every combination of hyperparameters in a defined search space. The set of best hyperparameters was trained on the entire training set and evaluated on the test set. The AUROC was calculated based on the algorithms' predicted probability that the subject developed AKI. This process was repeated 50 times and a vertical averaging method was used to calculate the mean ROC curve and associated 95% confidence interval (CI) and the mean AUROC and associated 95% confidence interval.[8]

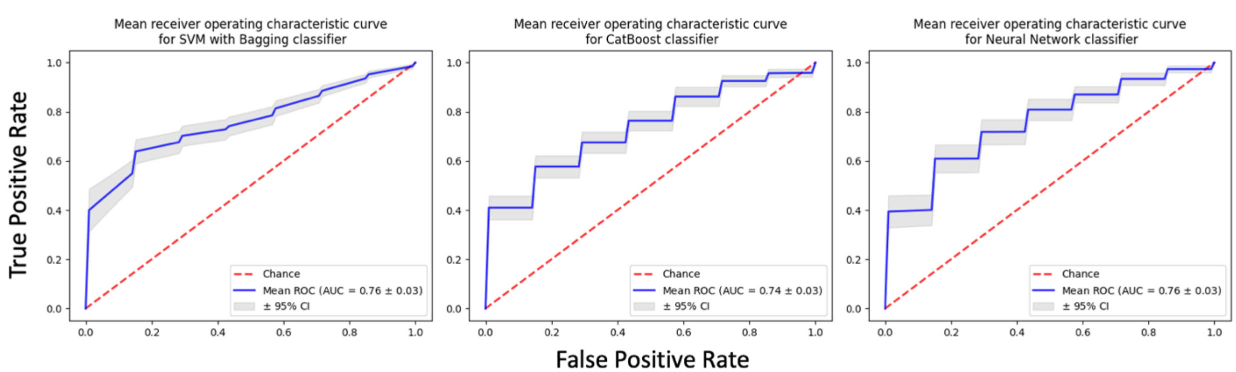

Figure 1 - Mean ROC curve for untrained data for 3 different machine learning algorithms (from left to right: SVM ensemble with bagging, CatBoost and fully connected neural network) trained on PuO_2, BMI, and baseline creatinine data.

Results: Figure 1 shows the mean ROC curve for each algorithm. The average ($\pm$ 95% CI) AUROC was 0.76$\pm$0.03, 0.74$\pm$0.03, and 0.76$\pm$0.03 for the SVM with bagging, CatBoost and Neural Network classifiers, respectively.

Discussion: This research shows that machine learning algorithms trained with intraoperative PuO_2 data can reliably identify patients who will develop post-operative AKI compared to urinary biomarkers. These algorithms could be deployed in real time and are associated with a relatively low-cost device. One of the major limitations of this research is the small sample size. However, it is likely that as more data is collected the performance of the algorithm will improve as the underlying true distributions of PuO_2 in patients with and without AKI are clearer.

References:

1. Dasta JF et al. *Nephrol Dial Transplant*. 2008;23(6):1970-1974.
2. Moledina DG et al. *Semin Nephrol*. 2018;38(1):3-11.
3. Liu KD et al. *Clin J Am Soc Nephrol*. 2020;15(12):1838-1847.
4. Rizvi MS et al. *J Appl Lab Med*. 2017;2(3):386-399.
5. Evans RG et al. *Am J Physiol-Regul Integr Comp Physiol*. 2014;306(1):R45-R50.
6. Silverton NA et al. *Anesthesiology*. 2021;135(3):406-418.
7. Dorogush AV et al. Published online 2018.
8. Fawcett T. *Pattern Recognit Lett*. 2006;27(8):861-874.