

# Title: Continuous Intraoperative Data Analysis Using Machine Learning Reveals Multiple Parameters to Predict Post-CABG Renal Failure

## Authors:

Keith A. Dufendach, M.D.; Willa Potosnak; Anthony Wertz, M.S.; Kyle Miller, Ph.D.; Artur Dubrawski, Ph.D.; Arman Kilic, M.D.

## Purpose:

Renal failure is a frequent complication following cardiac surgery, yet intraoperative contributors to postoperative renal failure remain incompletely understood. The purpose of this study is to utilize machine learning techniques to identify intraoperative parameters that contribute significantly to the development of postoperative renal failure following coronary artery bypass grafting (CABG).

## Methods:

3,484 patients who underwent isolated CABG with the use of cardiopulmonary bypass were propensity matched in a 4:1 fashion according to STS predicted risk of renal failure yielding 75 patients who developed postoperative renal failure (RF) and 287 without postoperative renal failure (NRF). Intraoperative data was extracted from the anesthesia record including hemodynamic measurements, medication and fluid administration, and ventilator settings. These data were plotted and compared using a Kolmogorov-Smirnov statistic. Using identified features of interest, machine learning classifier models (naïve bayes, logistic regression, random forest, extra trees, K-nearest neighbors, and quadratic discriminant analysis) were tested to determine predictive utility.

## Results:

STS Predicted risk of renal failure was similar in the matched cohorts (6.00% vs 6.00%,  $p = 0.555$ ) A total of 70 intraoperative parameters were compared using the Kolmogorov-Smirnov statistic revealing 20 parameters which were statistically different between RF and NRF groups (Figure 1). Predictive intraoperative parameters in decreasing order of significance included systolic arterial pressure, pulse pressure, heart rate, tidal volume, mean arterial pressure, systolic pulmonary artery pressure, diastolic arterial pressure, fractionated inspired  $O_2$ , near-infrared spectroscopy cerebral oxygenation (left), mean pulmonary artery pressure, near-infrared spectroscopy cerebral oxygenation (right), bispectral index value, diastolic pulmonary artery pressure, and systemic venous  $O_2$  saturation (Table 1). The Extra Trees classifier machine learning model resulted in the best performance amongst the trialed machine learning models when limiting to intraoperative risk factors with an area under receiver-operating-characteristic curve that improved by 0.111 when compared to logistic regression.

## Conclusions:

After accounting for baseline preoperative risk, there are multiple intraoperative parameters that significantly impact rates of postoperative renal failure in isolated CABG. Utilizing machine learning to identify such patterns and quantify their impact on postoperative renal failure can help in developing targeted efforts to mitigate risk.

Table 1. Features of interest used in the machine learning models for development of renal failure. Note that a  $-\log_{10}(\text{p-value})$  less than -1.30 indicates statistical significance ( $p < 0.05$ ).

Intraoperative Features of Interest	$-\log(\text{p-value})$	Mean Difference
Systolic arterial pressure (mmHg)	-22.30	0.41
Pulse pressure - arterial (mmHg)	-15.17	1.10
Heart rate (beats/minute)	-9.19	3.41
Tidal volume (mL)	-7.95	11.08
Mean arterial pressure (mmHg)	-6.10	0.76
Systolic pulmonary artery pressure (mmHg)	-4.79	0.31
Diastolic arterial pressure (mmHg)	-4.49	0.70
Fractionated inspired O <sub>2</sub> (%)	-3.92	1.43
NIRS Cerebral oxygenation - Left (%)	-3.65	0.23
Mean pulmonary artery pressure (mmHg)	-3.65	0.23
NIRS Cerebral oxygenation - Right (%)	-2.43	1.90
Bispectral index value	-2.01	1.28
Diastolic pulmonary artery pressure (mmHg)	-2.01	0.61
Systemic venous O <sub>2</sub> saturation (%)	-1.62	1.12

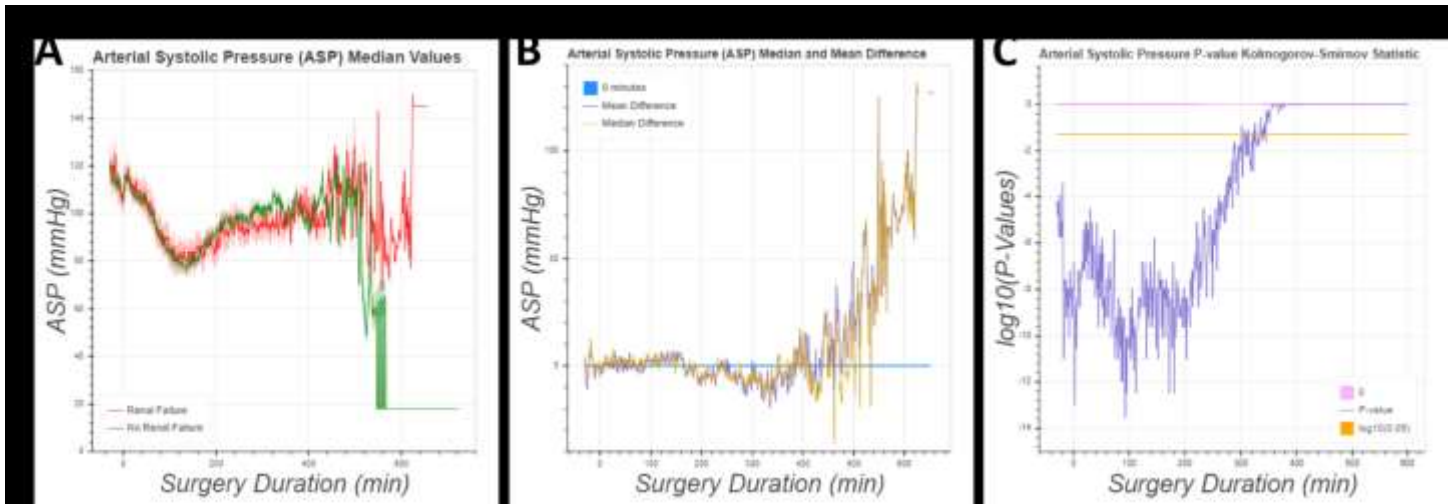


Figure 1. Example intraoperative data plots of systolic arterial pressure. A) Median arterial systolic blood pressure recordings in RF patients (red) and NRF patients (NRF). B) Mean and median difference (RF minus NRF) in systolic blood pressure at each timepoint. Points below 0 indicate RF had lower systolic pressures at that individual timepoint. C) Plot of  $-\log_{10}(p\text{-value})$  at each individual timepoint. The yellow line indicates the cutoff for significance ( $p = 0.05$ ;  $-\log(0.05) = -1.30$ ). Plotted points below the yellow line indicate timepoints where systolic arterial pressure was significantly different between RF and NRF patients.

Multiple Choice Question:

The task of predicting whether or not a patient will develop postoperative renal failure using a propensity matched training dataset of patients who either went on to develop renal failure or did not is classified as which of the following machine learning problems?

- 1) Unsupervised classification
- 2) Supervised classification
- 3) Unsupervised regression
- 4) Supervised regression

Bibliographic reference:

Kilic AK, et al. Predictive Utility of a Machine Learning Algorithm in Estimating Mortality Risk in Cardiac Surgery. Ann Thorac Surg. 2020;1811-1819.





# Continuous Intraoperative Data Analysis Using Machine Learning Reveals Multiple Parameters to Predict Post-CABG Renal Failure

W. Potosnak<sup>1</sup>, K. Dufendach<sup>2</sup>, A. Wertz<sup>1</sup>, K. Miller<sup>1</sup>, A. Dubrawski<sup>1</sup>, and A. Kilic<sup>2</sup>

1. Carnegie Mellon University, School of Computer Science, Auton Lab, Pittsburgh, PA USA

2. University of Pittsburgh Medical Center, Division of Cardiac Surgery, Pittsburgh, PA USA

## INTRODUCTION

- Coronary artery bypass grafting (CABG) is the most commonly performed cardiac surgery operation in the United States, with an estimated 370,000 procedures performed each year [1].
- Renal injury or failure following cardiac surgery is associated with worse outcomes including increased mortality [2].
- The Society of Thoracic Surgeons Adult Cardiac Surgery Risk Calculator uses preoperative patient characteristics to predict new postoperative renal failure [3].
- Intra-operative risk factors for development of renal failure are undefined and elucidating these parameters may provide a target for lowering the overall rate of renal failure following CABG.

## AIM

The purpose of this study is to utilize machine learning techniques to identify intraoperative parameters that contribute significantly to the development of postoperative renal failure following CABG and predict postoperative renal failure based on these parameters.

## METHODS

- 3,484 patients who underwent isolated CABG at a single tertiary care center were propensity matched in a 4:1 fashion according to STS predicted risk of postoperative renal failure resulting in 287 patients who did not develop renal failure (NRF) and 75 patients who did (RF). The STS predicted risk of renal failure was 6.00% in both groups (p = 0.555).
- Continuous intraoperative data were gathered retrospectively from the anaesthesia record and included hemodynamic information such as heart rate, arterial blood pressure, central venous pressure, pulmonary artery pressure, as well as additional information such as ventilator settings, temperature, and medication or fluid administration.
- Each operation was split into four phases: preoperative, pre-bypass, cardiopulmonary bypass, and post-bypass. Average mean arterial pressure and standard deviations were generated for each phase and were included as features in the dataset.
- Multiple machine learning algorithms were tested with this dataset using 10-fold cross validation with stratified folds and their classification performance was measured using area under the receiver operating characteristic curves (ROC-AUC). The algorithms tested include logistic regression, extremely randomized trees (or extra trees), random forest, naïve bayes, extreme gradient boosting, linear discriminant analysis, support vector machine, and k-nearest neighbors.

## RESULTS

- Preoperative characteristics were similar between groups with the exceptions of body surface area (2.09 NRF vs 2.02 RF, p = 0.049), alcohol use (66.9% vs 54.7%, p = 0.049), and need for supplemental oxygen (3.1% vs 5.3%, p = 0.034).
- Table 1 shows several intraoperative variables which were significantly different between RF and NRF patients. Figure 1 shows a time series comparison of mean arterial pressure providing a rationale for use in machine learning models.
- The machine learning model based on logistic regression showed the highest mean ROC-AUC, also known as c-index, with a mean ROC-AUC of 0.648 using only intra-operative data (Figure 2).
- Figure 3 shows a comparison of RF versus NRF patients and shows the power of machine learning to identify a subset of patients who have a high rate of renal failure based on intraoperative parameters despite a low STS risk score.

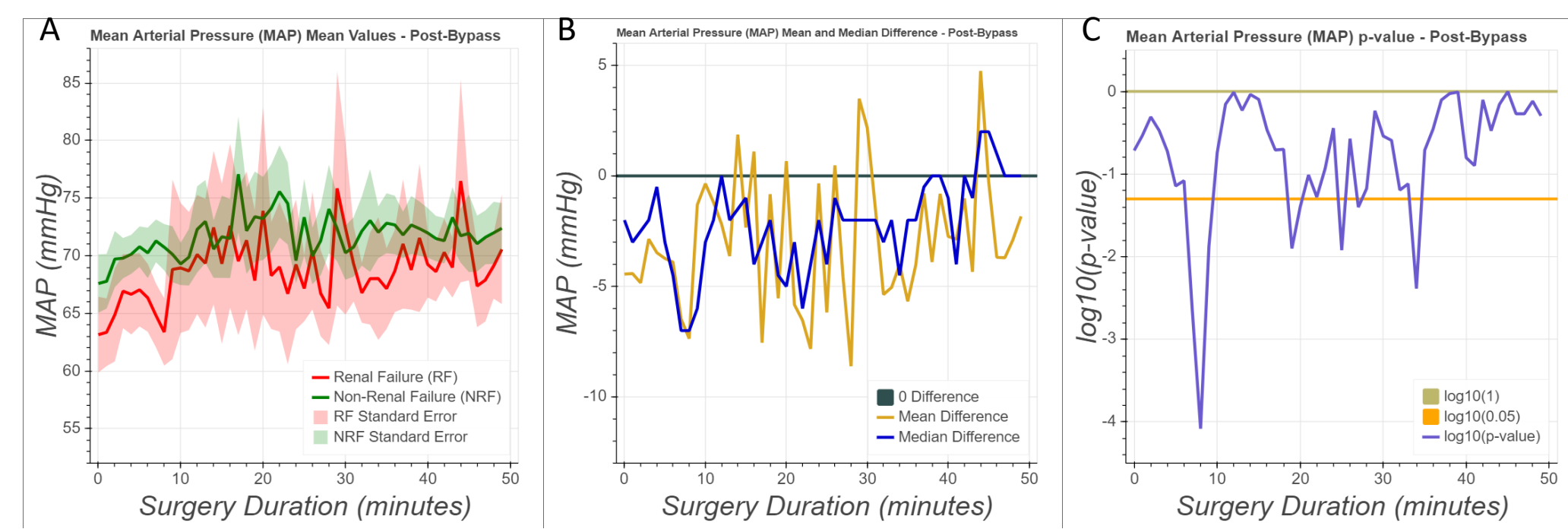


Figure 1. (A) Time series comparison of mean arterial pressure for the first 50 minutes post-bypass between renal failure and non-renal failure patients. (B) Median and mean difference between renal failure and non-renal failure patients (RF minus NRF). (C) Time series log(P-value) for distribution of mean arterial pressure between RF and NRF patients, less than -1.3 indicates statistical significance (p < 0.05).

Abbreviations:  
MAP = mean arterial pressure

Preoperative			
Feature	RF Mean ± SD	NRF Mean ± SD	P-Value
Tidal Volume - Exhaled SD	122.48 ± 49.42	141.85 ± 51.26	0.0061
Mean Arterial Pressure SD	10.72 ± 6.49	12.59 ± 8.17	0.0071
Diastolic BP SD	7.98 ± 4.89	9.84 ± 7.19	0.0187
Tidal Volume - Exhaled	474.21 ± 87.6	503.53 ± 102.78	0.0256
NIRS Cerebral Oxygenation-R	63.99 ± 10.86	67.35 ± 10.93	0.0539
Heart Rate SD	11.85 ± 8.35	10.55 ± 8.04	0.0627
Systolic BP SD	15.75 ± 9.52	17.76 ± 10.98	0.0767
PEEP SD	1.66 ± 0.93	1.52 ± 1.03	0.08
Respiratory Rate	12.58 ± 2.7	11.85 ± 2.07	0.1301
Pulse Pressure - Blood SD	11 ± 7.03	12.18 ± 7.82	0.1421
Pre-cardiopulmonary bypass			
Feature	RF Mean ± SD	NRF Mean ± SD	P-Value
Peak Inspiratory Pressure	19.95 ± 4.2	18.71 ± 4.3	0.0143
Tidal Volume - Exhaled SD	54.08 ± 31.24	66.4 ± 40.33	0.0275
Ambient Pressure SD	0.13 ± 0.29	0.35 ± 0.65	0.0282
Pulmonary Artery Mean SD	8.87 ± 9.88	4.93 ± 8.06	0.0419
NIRS Cerebral Oxygenation-R	64.69 ± 10.97	69.17 ± 11.23	0.044
PEEP	4.16 ± 1.56	3.62 ± 1.39	0.0443
Pulmonary Artery Systolic SD	10.39 ± 10.01	6.3 ± 7.84	0.0625
NIRS Cerebral Oxygenation-L	65.41 ± 10.88	69.83 ± 10.95	0.0669
Pulmonary Artery Diastolic std	8.22 ± 10.32	4.2 ± 8.02	0.0687
Tidal Volume - Exhaled	475.17 ± 97.67	505.95 ± 112.39	0.0983
Cardiopulmonary bypass			
Feature	RF Mean ± SD	NRF Mean ± SD	P-Value
NIRS Cerebral Oxygenation-R	59.23 ± 8.46	62.17 ± 9.36	0.1185
NIRS Cerebral Oxygenation-L	60.36 ± 8.22	62.49 ± 9.28	0.1487
Heart Rate - Pleth	82.69 ± 33.12	82.91 ± 37.12	0.1777
Ambient Pressure	734.58 ± 5.21	733.99 ± 10.77	0.2091
Temp #2	1 ± 0	1 ± 0	0.2147
Temp #2 SD	0 ± 0	0 ± 0	0.2147
SpO2 SD	4.43 ± 6.75	3.18 ± 4.97	0.2205
Heart Rate - Art	69.92 ± 29.47	67.82 ± 31.85	0.2287
Peak Inspiratory Pressure	12.37 ± 11.16	11.47 ± 11.05	0.2337
Tidal Volume - Exhaled	414.63 ± 224.04	407.88 ± 275.34	0.2532
Post-bypass			
Feature	RF Mean ± SD	NRF Mean ± SD	P-Value
Peak Inspiratory Pressure	22.13 ± 4.92	20.86 ± 5.15	0.0056
Tidal Volume - Exhaled	496.36 ± 122.5	524.44 ± 119.85	0.0076
NIRS Cerebral Oxygenation-L	59.18 ± 9.09	64.37 ± 10.66	0.0207
Arterial Diastolic Pressure SD	15.16 ± 8.9	15.73 ± 11.42	0.0339
Mean Arterial Pressure	69.64 ± 6.27	72.25 ± 10.59	0.035
NIRS Cerebral Oxygenation-R	58.15 ± 10.2	63.62 ± 11.27	0.0421
Pulmonary Artery Mean SD	14.1 ± 25.46	10.8 ± 23.19	0.0486
Heart Rate - Pleth SD	12.58 ± 13.77	9.36 ± 10.4	0.0545
Arterial Systolic Pressure	100.21 ± 9.94	103.59 ± 11.18	0.0552
Respiratory Rate	13.79 ± 3.78	12.9 ± 3.49	0.0601
Pulmonary Artery Diastolic SD	13.79 ± 25.84	10.53 ± 23.6	0.0749

Table 1. Top 10 overall features for renal failure and non-renal failure patients separated by phase of surgery. Red line marks statistical significance (p < 0.05), indicating features with significant deviation between classes.

Abbreviations:  
BP = blood pressure  
NIRS = near infrared spectroscopy  
NRF = non-renal failure  
PEEP = positive end-expiratory pressure  
RF = renal failure  
SD = standard deviation  
SpO2 = systemic oxygen saturation

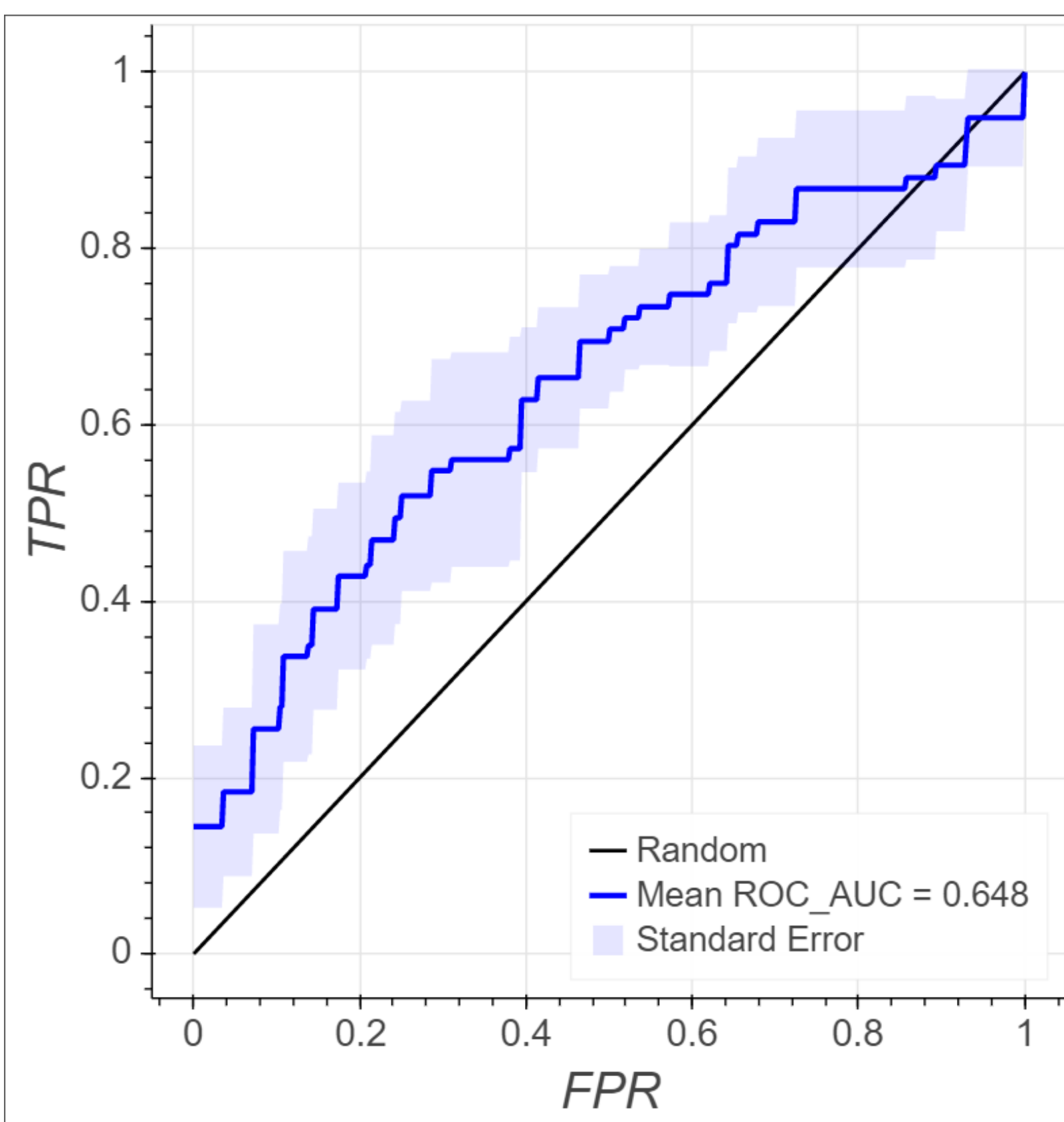


Figure 2. Receiver operating characteristics curve using logistic regression machine learning model for development of postoperative renal failure based only on intraoperative data.

Abbreviations:  
TPR = true positive rate  
FPR = false positive rate  
ROC\_AUC = area under the receiver operating characteristic curve (c-index)

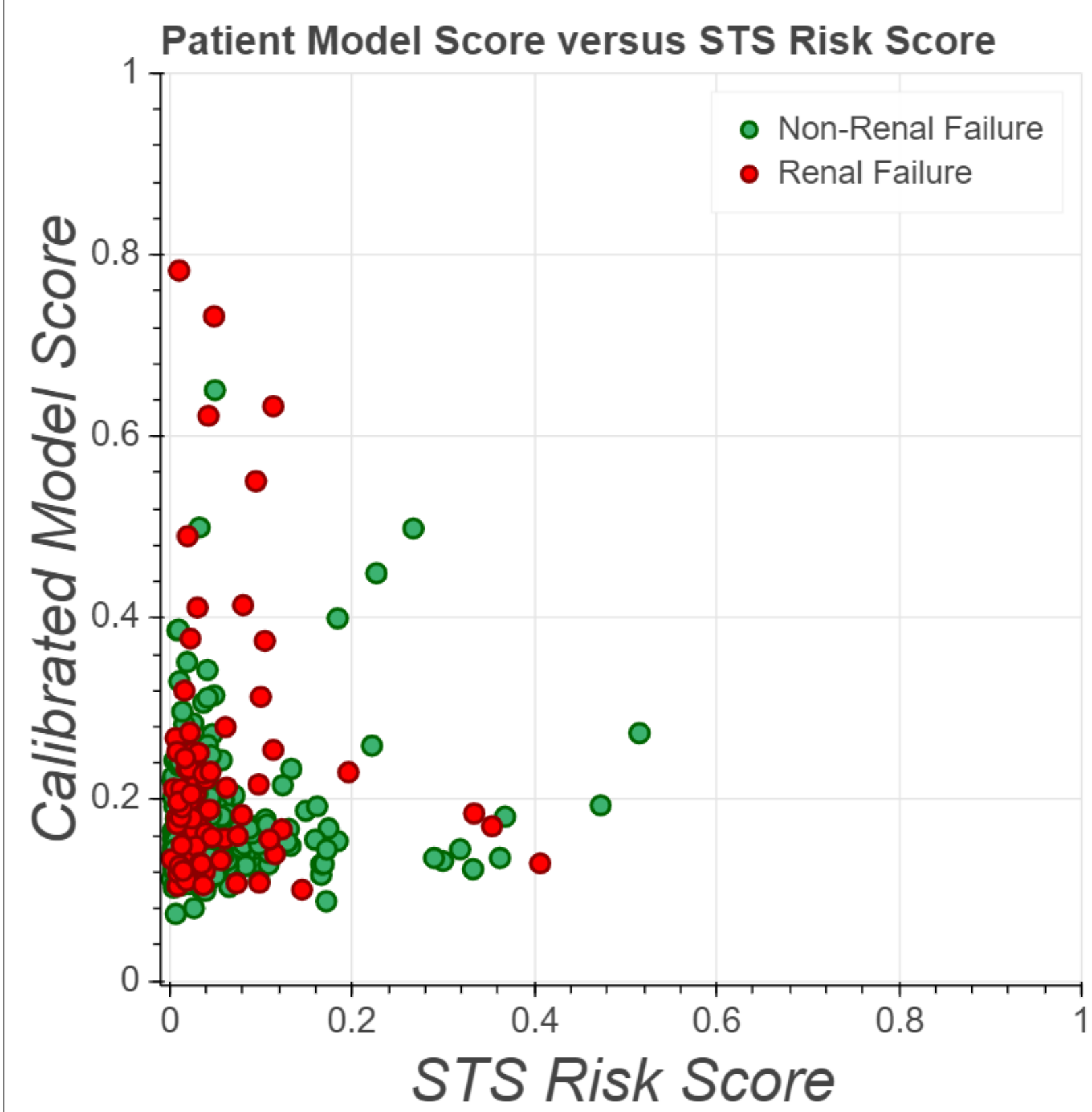


Figure 3. Scatter plot of patients' machine learning model score based on intraoperative data only versus STS risk score for renal failure based on preoperative characteristics. Patients near the top of the y-axis represent a subgroup with high risk of renal failure based on the machine learning model despite a low STS score.

Abbreviations:  
STS = Society of Thoracic Surgeons

## CONCLUSIONS

- Machine learning in cardiac surgery allows providers to discover new insights from datasets that were previously too large or complex for analysis.
- Continuous intraoperative data gathered from patients undergoing CABG revealed potential targets for early, intraoperative intervention to prevent the development of postoperative renal failure.
- Intraoperative data analysis with machine learning identified a subset of patients who are at higher risk of postoperative renal failure than that predicted by the STS calculator based only on preoperative characteristics, resulting in a subgroup who may benefit from early postoperative care aimed specifically at renal protection.
- Additional machine learning algorithm optimization and feature engineering are necessary to improve the sensitivity and specificity of the predictive capability of the algorithm.

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## CONTACT INFORMATION

Arman Kilic, M.D.  
Division of Cardiac Surgery, University of Pittsburgh Medical Center  
200 Lothrop Street, Suite C-700, Pittsburgh, PA 15213, USA.  
Phone: (412) 648-6200 | Fax: 412-692-2184  
Email: kilica2@upmc.edu)