A Predictive Model for Sub-therapeutic Vancomycin Troughs in Adults

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Background

- Exposure to vancomycin trough concentrations of <10 mg/L can produce strains of vancomycin-intermediate or resistant *Staphylococcus aureus (S. aureus)*
- Despite guideline recommendations to target vancomycin troughs of 10 to 20 mg/L, sub-therapeutic vancomycin troughs occur in upwards of 40% of patients treated with vancomycin
- The goal of this study is to develop a predictive model to identify adult patients likely to have initial sub-therapeutic vancomycin troughs

Methods

Study Design

- Cohort study at Cleveland Clinic Health System (CCHS)
- Time frame: September 1st 2020 to August 31st 2021

Inclusion Criteria

- Adults admitted to a CCHS hospital
- The first course of vancomycin therapy during an eligible admission with a steady state trough
- Ordered a pharmacy to dose vancomycin consult

Exclusion Criteria

- Unable to capture critical data points
- Less than four doses of vancomycin for initial regimen
- Supra-therapeutic steady state troughs
- Pregnancy, cystic fibrosis, creatinine clearance less than 30 mL/min, received vancomycin dosed by levels, or on dialysis during vancomycin therapy

Statistical Analysis

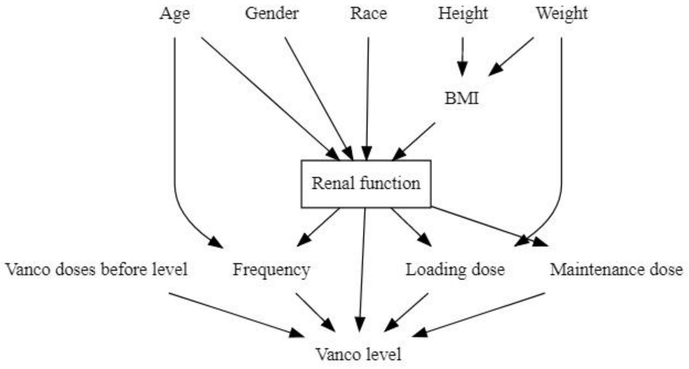
- A causal diagram for vancomycin trough levels was prepared
- A predictive model using KNN regression was developed, with predictors selected on the basis of the causal diagram, to predict a sub-therapeutic vancomycin trough level
- The model was validated using 10-fold cross validation

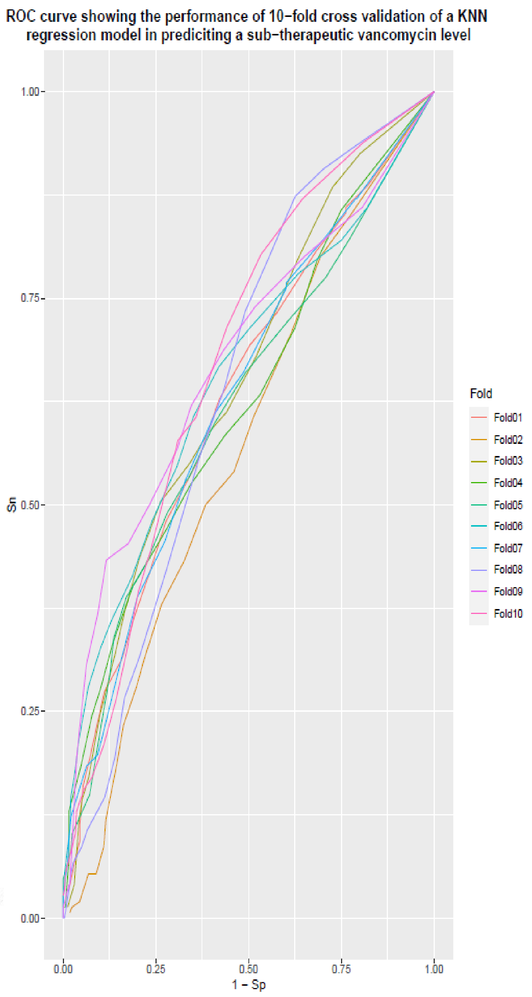
Results

	Sub-therapeutic n = 495	Therapeutic n = 1123	P – value
Age, years	50.37 (16.86)	58.79 (13.61)	<0.001
Sex			0.738
Male	307 (62.0)	685 (61.0)	
Female	188 (38.0)	438 (39.0)	
Race			0.314
White	355 (71.7)	842 (75.0)	
Black	97 (19.6)	203 (18.1)	
Other	43 (8.7)	78 (6.9)	
BMI, kg/m^2	28.10 (8.41)	30.84 (10.55)	<0.001
Loading Dose, yes	44 (8.9)	154 (13.7)	0.008
Dose, mg/kg	14.50 (1.92)	14.28 (2.14)	0.057
Number of doses before trough	4.97 (1.44)	4.91 (1.52)	0.522
Regimen Guideline Adherence			0.047
Yes	403 (81.4)	863 (76.8)	
No	92 (18.6)	260 (23.2)	
ID Consult, yes	191 (38.6)	389 (34.6)	0.142

All data reported as n (%) or mean (standard deviation), as appropriate

Vancomycin Trough Causal Diagram





Results Continued

- Accuracy of vancomycin dosing guideline in achieving a therapeutic vancomycin level was 0.59.
- The predictive model performed better. The mean area under the ROC curve for the 10-fold cross validation was 0.65. The mean accuracy of the model from 10-fold cross validation was 0.69

Discussion

- A predictive model based on a causal diagram for vancomycin trough levels was able to predict a sub-therapeutic vancomycin level more accurately than institutional vancomycin dosing guidelines.
- This predictive model could be a useful adjunctive tool in initiating appropriate vancomycin regimens and avoiding the development of *S. aureus* resistance in adult patients.
- Limitations
  - Creatinine clearance is a less than perfect marker of renal function.
  - Definitions of sub-therapeutic, therapeutic, and supra-therapeutic troughs
  - Excluding patients with supra-therapeutic troughs from the model

References

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