The role of “vancokinemia” in the non-critical population as a diagnostic and prognostic predictor of acute kidney injury

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Background

There have been few studies to evaluate the monitoring of plasmatic concentrations of vancomycin in septic patients and their association with acute kidney injury (AKI) and death. This study aimed to evaluate the prevalence of adequate, subtherapeutic, and toxic serum concentrations of vancomycin in hospitalized septic patients and to associate the adequacy of therapeutic monitoring with clinical outcomes.

Methods

This was a prospective observational cohort study of adult patients diagnosed with sepsis defined using the quick SOFA and admitted to four wards at the Clinics Hospital of Botucatu Medical School (two clinical and two surgical) during August 2016 to July 2017. Vancomycin was used according to the institution’s protocols: loading dose of 25 mg/kg and maintenance of 15 mg/kg, with dosing intervals of 12/12–96/96 hours, depending on the serum concentration of the anti-microbial.

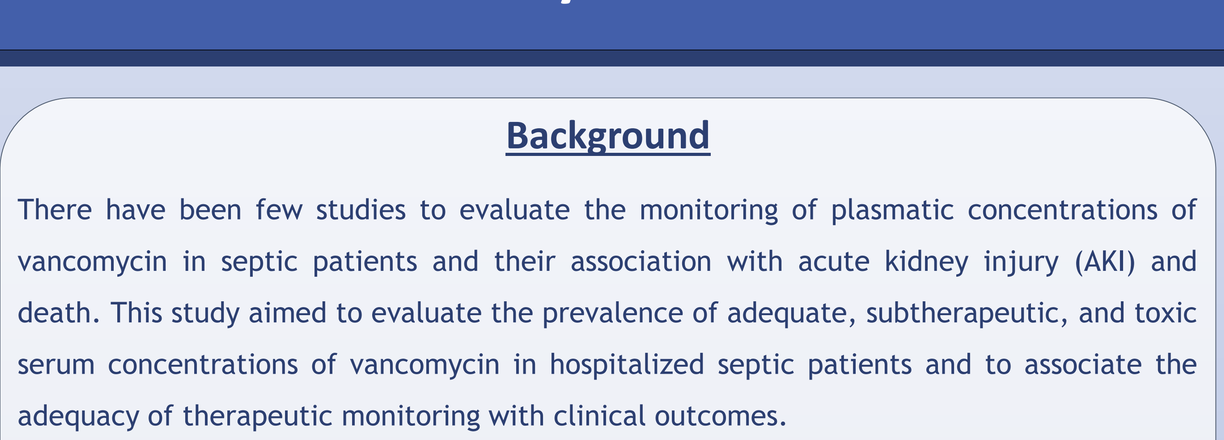

Figure 1 Flow diagram of patients included and excluded.

The study was approved by the local research ethics committee and registered in the Brazilian Registry of Clinical Trials (ReBEC) under number RBR-4zrwtz.

Results

We included 135 patients from clinical and surgical wards, of which 94.1% had serum concentrations of vancomycin measured during the use of the antimicrobial. Of these, 75.6% received adjustments in dosage and 59.3% presented a toxic serum concentration of vancomycin. The mean higher value for serum concentration was 22.07±14.77mg/L, 27.4% of the patients presented with AKI, of which KDIGO stage 1 was the most frequent (54.05%), and 20.7% evolved to death.

Table 3 Cox Regression of Variables Associated with the Presence of AKI in Patients Using Vancomycin Hospitalized in Clinical and Surgical Wards

Variables	HR	CI	*p*-value
Number of adjustments	1.17	0.91–1.5	0.21
Vasoactive drug	1.004	0.96–1.2	0.953
Mechanical ventilation	1.007	0.97–1.118	0.947
Attack dosage (mg)	1.001	1.000–1.002	0.87
Vancomycin T4–T6 (mg/L)	**1.064**	**1.003–1.128**	**0.038**

Notes: T4–T6, serum concentration between the fourth and sixth days of usage of vancomycin (96–144 hours). Values in bold denote significance.

In Cox regression analysis, serum concentration of vancomycin during 96–144 hours (T4–T6, HR 1.06; p=0.038) was identified as the only risk factor for AKI. ROC-curve analysis showed that serum concentration >21.5 mg/L between the fourth and sixth days was a good predictor of AKI, with area under the curve of 0.8 (95% CI 0.62–0.98), sensitivity of 81.1%, specificity of 73.7%, and preceding diagnosis of AKI by at least 3 days (AKI happened on average at the ninth day of vancomycin use). The free time for the development of AKI was smaller than the group with serum concentrations <21.5 mg/L (log rank 0.026)

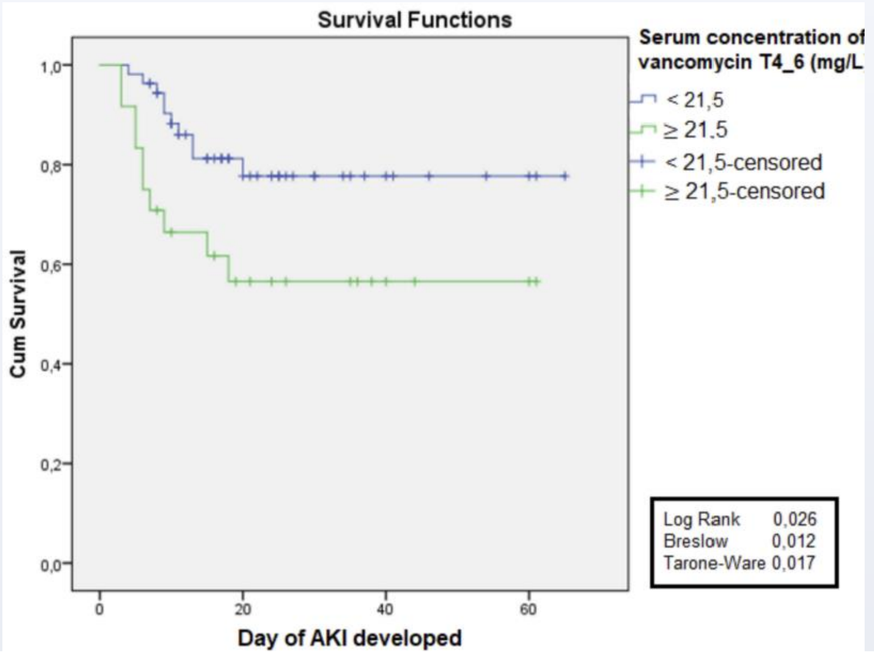

Figure 3 Free time for acute kidney injury (AKI) according to serum concentration (cutoff 21.5 mg/L) during T4–T6 days (96–144 hours) for use of vancomycin in septic patients in clinical and surgical wards.

In Cox regression, it was observed that serum concentration of vancomycin between the fourth and sixth days (HR 1,078, p=0.039), was the sole predictor of death. The free time curve for death, based on the cutoff values obtained by the ROC curve for 4–6 days, it was observed that free time for death was smaller for the group with serum concentration >21.5 mg/L (log rank 0.006).

Table 6 Cox Regression of Variables Associated with Death in Patients Using Vancomycin Hospitalized in Clinical and Surgical Wards

	HR	CI	p-value
Diabetes mellitus	2.434	0.637–9.294	0.193
SOFA score	1.169	0.99–1.38	0.066
Serum concentration, T4–T6 days (mg/L)	**1.078**	**1.004–1.157**	**0.039**
Age	0.992	0.959–1.025	0.63
Follow-up with nephrologist (due to AKI)	0.934	0.243–3.584	0.92

Notes: T4–T6, serum concentration between the fourth and sixth days of usage of vancomycin (96–144 hours). Values in bold denote significance.
Abbreviation: AKI, acute kidney injury.

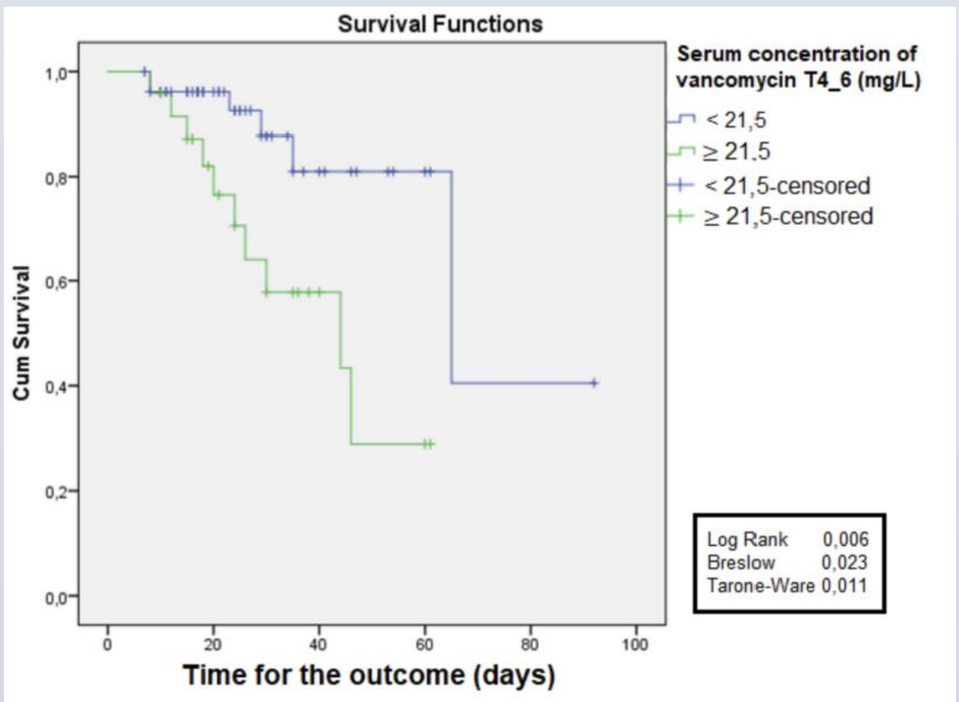

Figure 4 Free time for death outcome according to serum concentration (cutoff 21.5 mg/L) during T4–T6 for vancomycin in patients hospitalized in surgical and clinical wards. T4–T6, serum concentration between the fourth and sixth days of usage of vancomycin (96–144 hours).

Conclusion

Serum concentration of vancomycin is an excellent predictor of AKI in patients admitted to wards, preceding the diagnosis of AKI by at least 72 hours. Toxic concentrations of vancomycin are associated with AKI, and AKI was a risk factor for death. Also, serum concentration of vancomycin >21.5 mg/L was the only variable associated with death in the Cox model.