



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Cardiology

**Manuscript NO:** 40797

**Title:** Incidence and Risk Factors for Potentially Suboptimal Serum Concentrations of Vancomycin during Cardiac Surgery

**Reviewer’s code:** 03650328

**Reviewer’s country:** Canada

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-10

**Date reviewed:** 2018-07-12

**Review time:** 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Incidence and Risk Factors for Potentially Suboptimal Serum Concentrations of Vancomycin during Cardiac Surgery by Cotogni et al. In this study, leveraging samples collected in a previous prospective study, the authors examine the frequency of



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subtherapeutic vancomycin levels intraoperatively in adult patients undergoing cardiac surgery. The study is well-written and clearly presented. 1. In the Abstract Conclusion, mention the subgroups that the authors have identified as being at risk for suboptimal vancomycin levels. I would also include the result that infusion duration did not correlate with frequency of suboptimal levels. 2. Are the headings for Table 1 correct? In the Abstract, it is stated that the Cmax and AUC were higher in the patients with no level <10 mg/L. 3. Given that the number of outcomes (3 SSIs) is too small for statistical comparison, can you estimate the number of patients required for a future study to determine the impact of subtherapeutic vancomycin levels on frequency of SSIs (i.e. will this require a multi-centre study)? 4. Since the 10 mg/L level was chosen arbitrarily, please report the frequency of all vancomycin levels measured (10, 20, 30 and 40 mg/L) for the cohort. 5. Why was >70 years chosen as the cut-off for age at surgery? 6. Similarly, what is the justification for CrCl >70? 7. Define what you mean by 'fluid balance' and infusion 'stopped vs. non-stopped' in Table 2. 8. Is the timing of the low level(s) more important than the frequency? Was this examined? 9. For Figure 2, in the legend, can you please include what the target time was. 10. In the Abstract, I think it is worth mentioning, in addition to the number who had at least 1 subtherapeutic level, that 54 patients had >=5 subtherapeutic levels since this is likely more relevant for the development of resistance than just having 1-2 low levels.

## INITIAL REVIEW OF THE MANUSCRIPT

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**Manuscript NO:** 40797

**Title:** Incidence and Risk Factors for Potentially Suboptimal Serum Concentrations of Vancomycin during Cardiac Surgery

**Reviewer’s code:** 00227341

**Reviewer’s country:** Italy

**Science editor:** Ying Dou

**Date sent for review:** 2018-07-19

**Date reviewed:** 2018-07-25

**Review time:** 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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**SPECIFIC COMMENTS TO AUTHORS**

The Authors have investigated the incidence and risk factors for vancomycin concentrations under 10 mg/L during cardiac surgery. Already other authors have reported that low concentrations are associated with treatment failure and emergence



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of resistance. In this study the Authors have reported an incidence of intraoperative potentially suboptimal concentrations of vancomycin in almost 50% of these patients. The multivariate analysis identified female gender, BMI >25, and creatinine clearance above 70 mL/min as risk factors for vancomycin level under 10 mg/L. This report is interesting, despite that the authors arbitrarily have taken into consideration vancomycin level of 10 mg/L as cut-off for potentially suboptimal serum concentrations in the case of antimicrobial prophylaxis, referring to the level reported in the literature in the case of antimicrobial therapy. On the other hand, in literature there are no data on the optimal level of vancomycin concentration for prophylactic purposes. I suggest some changes: - it could be useful to introduce a table on the population characteristics as the reference article is not available for everyone on pubmed - page 7, line 18 please specify the acronym SSI - page 8 line 14 MRSA o MSSA? - page 8, line 28 : I would suggest inserting two ROC charts in reference to what is written "Vancomycin PK parameters were estimated and compared between above versus under 10 mg/L patient groups (Table 1): Cmax and area under the concentration-time (AUC) curve were significantly higher in the patients with no vancomycin level under 10 mg/L, while the apparent total body clearance (Cl) and the apparent volume of distribution during the terminal phase (Vd) were significantly higher in the patients with at least 1 episode of vancomycin concentration under 10 mg/L."

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