

PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine

Manuscript NO: 53366

Title: Ventilator-associated pneumonia in patients with cancer. Impact of multidrug resistant bacteria.

Reviewer's code: 04334222

Position: Editorial Board

Academic degree: MD

Professional title: Assistant Professor, Doctor, Instructor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Mexico

Manuscript submission date: 2019-12-16

Reviewer chosen by: Ying Dou

Reviewer accepted review: 2020-02-15 19:29

Reviewer performed review: 2020-02-18 16:44

Review time: 2 Days and 21 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

First, Original aspects: This study highlights the high percentage of Gram-negative bacteria, which allows the initiation of empiric antibiotic coverage for these pathogens. Second, this study demonstrate of empiric antibiotic coverage no impact on mortality related to MDRB. Third, the limitation of the study: the results are referral in only one center in Mexico City.

PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine

Manuscript NO: 53366

Title: Ventilator-associated pneumonia in patients with cancer. Impact of multidrug resistant bacteria.

Reviewer's code: 03342506

Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Mexico

Manuscript submission date: 2019-12-16

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-26 11:13

Reviewer performed review: 2020-03-04 05:44

Review time: 6 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Authors present a single center retrospective observational study from a cancer referral center looking at ventilator associated pneumonia in patients with cancer and impact of multi drug-resistant bacteria. The study is overall well presented and of some interest to clinicians and researchers in the field. The following issues should be addressed prior to considering the manuscript for publication: One of the primary findings is the association of LOS and VAP . This finding needs some explanation. Is this LOS BEFORE VAP? Otherwise, the reason for association would be explained by “effect-cause” bias (VAP causing increased LOS, rather than viceversa), The same comment is related to hospital LOS and duration of ventilation. Please clarify. Please consider specific suggestion for each section below: **ABSTRACT** **Methods:** Page 2 Line 17-18 needs to be rephrased “They were classified as those who developed or not VAP” to “they were classified as those who developed VAP versus those who did not”. Page 2 Line 19: “The presence of MDRB was recorded” is redundant as authors have mentioned this in the preceding sentence. “Outcome at 60-day was assessed” what were the assessed outcomes (primary & secondary)? **Conclusion:** “This study highlights the high percentage of Gram-negative bacteria, which allows the initiation of empiric antibiotic coverage for these pathogens.” This adds no new knowledge to the current literature available regarding microbiology of ventilator associated pneumonia. Lopez-Ferraz, C., et al. (2014). "Impact of microbial ecology on accuracy of surveillance cultures to predict multidrug resistant microorganisms causing ventilator-associated pneumonia." J Infect 69(4): 333-340. Thakuria, B., et al. (2013). "Profile of infective microorganisms causing ventilator-associated pneumonia: A clinical study from resource limited intensive care unit." J Anaesthesiol Clin Pharmacol 29(3): 361-366. “There was no impact on mortality related to MDRB.” This study does not have enough power due to

limitations of small sample size to establish this statement as a conclusion. The authors could potentially rephrase the statement as “In this single centered retrospective observational study, MRDB VAP was not directly linked to increased mortality at 60 days”. MAIN MANUSCRIPT Material and Methods: Page 5 Line 4: “Diagnosis of VAP” , authors should provide details on how they defined VAP for this study or provide a reference for standard diagnosis of VAP. Different than “pneumonia” present at the time of admission. Page 5 Line 5: “XRD” acronym is used for the first time without previously explaining it. Authors should also clearly state what were the primary and secondary outcomes. Results: Page 6 line 12: “736 patients were admitted to the ICU: 245 patients required MV for less than 48 h and 128 did not require intubation; 263 patients were included” Adding $245+128+263 = 636$, authors should explain this discrepancy. In the results section authors described that 38 patients had pneumonia as the primary diagnosis requiring mechanical ventilation and 32 patient had developed VAP. How did the investigators differentiate progression of pneumonia from development of new ventilator associated pneumonia is unclear in the manuscript. Page 7 Line 25 : Risk factors for VAP Authors do not provide any information about the immunocompromised state of the patient such as active chemotherapy, use of steroids etc. Discussion Page 8 Line 28: “An important finding in this study was that patients with VAP more frequently received broad-spectrum antibiotics (particularly cephalosporins, Tazobactam/Piperacillin, carbapenems, and Vancomycin).” This is expected, since this subset of patients was critically ill and required empiric antibiotics. They are understandably at a higher risk for longer intubation and length of stay in ICU. Further correlation with immunocompromised state (active chemotherapy and/or steroids) needs to be taken into account. Also correlation with degree of illness SOFA and charlson comorbidity index is not discussed. The median duration of mechanical ventilation is quite long with subsequent high



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mortality related to primary disease. It would be interesting to explain the palliative care and end of life care practices in your institution. **CONCLUSION** Page 10 Line 28: "It is important to highlight that the MDRB bacteria had no clinical impact in this group of patients." This study does not have enough power due to limitations of small sample size to establish this statement as a conclusion. **TABLES** Table 1: Instead of presenting clinical and demographic characteristics of all patients with mechanical ventilation during the study. Authors should consider presenting a table comparing the group of patients that developed ventilator associated pneumonia versus group of patients that did not developed ventilator associated pneumonia (VAP) to see if the groups were appropriately matched and important differences between the groups. Same comments for Table 2.

PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine

Manuscript NO: 53366

Title: Ventilator-associated pneumonia in patients with cancer. Impact of multidrug resistant bacteria.

Reviewer's code: 00608223

Position: Peer Reviewer

Academic degree: BM BCh, MD, MRCP, PhD

Professional title: Doctor, Reader (Associate Professor)

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Mexico

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Reviewer chosen by: Jie Wang

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Reviewer performed review: 2020-03-25 19:09

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The title reflects the main subject of the manuscript and the abstract and key words summarize/reflect the work described in the manuscript. In general the manuscript is coherently organized and presented, and language appropriate. A STROBE checklist is not uploaded as supporting file, but the features required by STROBE have mostly been included. The introduction adequately describes the background to the study regarding VAP, and some of the background on cancer patients in the ICU. It would have been good to see some additional epidemiology about these patients in the ICU setting - are they more commonly being admitted to ICU now compared to the past? What features might be dictating any changes? I ask this mainly because only half of the patients were thought to be in remission, with others having progressive disease - many ICU worldwide would not accept patients with progressive cancers for such invasive treatments at MV. This would help the authors contextualise their cohort with the rest of the world. The manuscript describes methods in adequate detail, this being a retrospective cohort study largely using routine data, however there are some improvements which could be made, mainly on the statistical approach. In this area the methods are not wholly consistent with the reporting of results, which requires clarification - for example the methods state "Variables with p values of <0.5 in the univariate analysis were included in the multivariate analysis", however in the table in which the multivariate results are shown there are many factors which appear to have $p < 0.5$ in the univariate that were not in the multivariate model. Why was logistic regression chosen over Cox regression and was there any assessment of collinearity in the data? Why was multivariate analysis only reported for mortality and not for development of VAP in its full form? The methods say it was done and there is some reporting in the text but I was not clear which factors went into the model. Ethics was

approved, in that a certificate was uploaded to the journal, but this is not stated in the actual manuscript - this should be added to the methods. The results largely concur with prior work in the field of general ICU patients indicating factors which may predispose to VAP and to mortality after an ICU stay. The organisms observed in the VAP patients were also fairly typical. The novel factor in this study was looking at cancer patients - I would be interested if cancer status (progressive or not) was a risk factor for VAP or death, and whether any treatment limitations were put in place (eg not for haemofiltration, not for CPR) in those with progressive disease. Reporting of VAP multivariate work could be better too as listed above. Tables are sufficient and appropriately illustrative of the paper contents. SI units were used. In the discussion the manuscript interprets the findings appropriately, but I felt the novelty of the cancer cohort was not enough - however to do this and really discuss the impact of cancer on ICU admission the team would need to analyse more around the cancer angles as described above. The limitations section is very brief and could be expanded. Referencing in the discussion was reasonable.